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HUMAN FACTORS IN PARASITE ECOLOGY[1]

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MAN, in spite of his cultural advances over the centuries, still harbors a greater variety of parasites than almost any other species of animal. Favorable to parasitic infection is his tendency to herd in concentrated groups and to wander widely over the earth's surface; favorable, also, is his close association with a wide variety of domesticated animals and the diversity of his food habits. Unfavorable, on the other hand, is his advancing culture with constantly improving standards of cleanliness, housing, food handling and excreta disposal.

Human factors especially unfavorable in parasite ecology are those consciously directed by man himself toward the destruction and control of his parasites. Great efforts have been made over the years with only a moderate degree of success to find specific drugs that will rid the body of these invaders. In fact, so great is the need in the present national emergency for better drugs for the treatment of the malarial parasites that the energies of scores of scientists in this country are being directed toward their discovery. Much effort has, also, been directed toward the control of parasites by the modification of human habits that are favorable for their dissemination. When transmission is directly from man to man of cysts

[1] Address of the retiring president, American Society of Naturalists, Dallas, Texas, December 31, 1941.

or eggs passed in the feces, as for example, with the intestinal protozoa and the common intestinal nematodes, attempts at control are directed toward the improvement of excreta disposal and of personal hygiene. Where infection takes place by the ingestion of the larval stages with the flesh of intermediate hosts, as with the large tapeworms, trichina and several of the flukes, control measures involve changes in food habits. For those parasites transmitted by the bites of blood-sucking insects as the malarial parasites, trypanosomes and the filariae, prevention consists of protection from insect bites and the eradication of specific vectors. For other parasites with still different methods of dissemination entirely different methods of control must be employed. For example, human infection with hydatid cysts comes only from the accidental ingestion of the eggs of a dog tapeworm, *Echinococcus granulosus;* the larval stages of the blood flukes (schistosomes) develop in snails and penetrate the human skin; and the guinea worm, *Dracunculus medinensis,* can reach the human body only by the ingestion of cyclops in which its larval stages have developed. In fact, for the spread of this worm most unusual human relations must be developed. Drinking water must be obtained from open wells or pools where the conditions are such that cyclops can multiply abundantly; and individuals with open sores on their feet and legs from which the guinea worm larvae are being extruded must wade or bathe in this water. It is no wonder, therefore, that the distribution of this parasite is very limited and that it can be easily controlled by improvement in the water supply (Moorthy and Sweet, 1936).

Human factors favorable in parasite ecology include, as already suggested, individual habits, such as soil pollution, the eating of raw food, carelessness in personal hygiene and inadequate protection from insects. There are, however, group, community or even national activities, over which the individual has little, if any, control, which in certain instances produce conditions which are

very favorable for the parasites. It is with examples of factors of this type that I wish to deal particularly in the present paper.

War is undoubtedly the most upsetting factor that can disturb the balance of human ecological relations; and no other factor is more favorable to the increased spread of human parasites. The late Hans Zinsser in his book, "Rats, Lice and History," has made a fascinating story of the relation of war to epidemics of louse-borne typhus fever. He has shown how disturbances of the ecological balance in the relations of this disease have produced great epidemics in armies and civilian populations that have altered the whole course of history. It has even been suggested that the prevalence of typhus in Spain has profoundly modified Hitler's plans and perhaps prevented an attack on Gibraltar, and it is not impossible that epidemics of this disease may greatly influence the final outcome of the fighting in Russia.

Many and varied, in fact, are the factors associated with war which combine to increase the spread of parasites. Crowded, insanitary conditions are produced in both armies and civilian populations; resistance is broken down by undernourishment in refugee groups; and mass migrations introduce parasites into new areas and bring groups of people into contact with new parasites. For example, the numerous infections of the blood fluke, *Schistosoma haematobium*, picked up by British soldiers in South Africa during the Boer War, cost the British Government millions of pounds in disability pensions. There is evidence, also, that Japanese soldiers in China are being infected in large numbers with certain helminth and protozoan parasites. The medical corps of the U. S. Army and Navy are greatly concerned over the dangers to American troops and civilians who are being sent to bases in tropical America and the Orient from malaria, amoebiasis, schistosomiasis and many other parasitic diseases.

Peace-time migrations of population are also of great

importance in spreading human parasites. The evidence is almost conclusive that hookworm disease was introduced into the southern United States and elsewhere in the Western Hemisphere by the importation of Negro slaves from tropical Africa. In this case, the white populations have suffered very severely from the infection, while the Negroes perhaps from centuries of exposure, seem to have some racial immunity. It has also been suggested (Stitt, 1928) that other parasitic diseases, including aestivo-autumnal malaria, rectal schistosomiasis, filariasis and dracontiasis, were first introduced into the Americas with the slaves; but of these, only pernicious malaria has succeeded in gaining a real foothold in the United States.

Constantly improving transportation facilities which are bringing all parts of the world closer and closer together are extending the range of human parasites. During the last century, numerous epidemics of bubonic plague have been started outside the endemic areas in the Orient by infected rats escaping from ships; during this period also yellow fever was repeatedly introduced into the United States from foci in tropical America and was apparently spread in this country, in certain instances at least, by infected mosquitoes carried in railway trains. Increased travel by automobile and airplane has added greatly to the danger of the introduction of human parasites into new areas. Already, automobile travel between the United States and Mexico is assuming large proportions, and with the completion of the new Pan American Highway large tropical areas will be brought much closer to the United States (Clark, 1928). Only constant vigilance of the health authorities will prevent the introduction of numerous parasites along this route.

The most striking example in recent years of the spread of a parasitic disease by modern transportation has been the dangerous situation produced by the introduction of *Anopheles gambiae* into Brazil. (See Rockefeller Foundation reports for 1938, 1939, 1940). This mosquito is

one of the most effective vectors of pernicious malaria in the world and is wide-spread in tropical Africa. It lives close to human habitations and bites man almost exclusively. Before 1930 it was not known in the Western Hemisphere. In that year, or perhaps shortly before, it was carried across the ocean, possibly by airplane or perhaps on one of the fast French destroyers working in connection with the French airlines between Dakar in West Africa and Natal on the hump of Brazil. In 1930 and 1931 there occurred in the vicinity of Natal an outbreak of malaria of unprecedented severity. By 1931 the gambiae mosquitoes had traveled 115 miles up the coast. Sporadic efforts were made to check their advance. By 1937 this invader had reached the well-populated valleys to the northwest of Natal, where in 1938 pernicious malaria reached epidemic proportions. In one valley there were over fifty thousand cases in that year, with over 90 per cent. of the population affected and a 10 per cent. mortality. As a result of the ravages produced by this mosquito normal occupations were so interrupted that almost the whole population of the affected areas was on government relief in 1939. Since it was entirely beyond the ability of the local governments to cope with this situation the National Government of Brazil with the help of the Rockefeller Foundation assumed responsibility in 1938. The first results of the control campaign were disappointing; but by the beginning of July, 1938, the army of defense had increased to over 2,000 men, including a large corps of specially trained doctors, technicians and inspectors. The frontiers of the infested areas were sharply defined by fumigation posts on all the outgoing roads. A ten-mile zone was established beyond the mosquito's furthest advance, and in it all possible breeding places were eliminated. By December, 1939, the advance of the enemy had been definitely checked and it had been pushed back to its main strongholds in the river valleys and on the narrow coastal shelf. Then during 1940 the defending army began advancing, using as its chief

weapons Paris green for all potential breeding places and spray insecticides for the fumigation of all buildings. By the end of the wet season of 1940 this mosquito had been restricted to the lower part of the largest infested valley and to a few other small scattered foci; and a final onslaught beginning in July of that year seems to have eliminated it entirely. This successful campaign has been carried out at a cost for actual control measures of well over $2,000,000. Constant vigilance and the expenditure of great effort and large sums of money will be necessary to prevent further introductions of this mosquito into the Western Hemisphere, especially if intercourse with tropical Africa should greatly increase. So the gambiae mosquito vies with Adolf Hitler as a menace to South America from bases on the African coast.

The literature on the epidemiology of malaria contains numerous examples of situations where human activities of a variety of types have produced conditions favorable for the breeding of the mosquito vectors. The island of Trinidad in the British West Indies has furnished two such examples. Several years ago the increase of malaria in the employees of an American company that held a concession on the island became such a problem that a careful study of the situation was made. It was found that the mosquitoes were breeding extensively in the water that collected in the hoof prints made by a herd of goats that had been brought in to furnish a milk supply for the children. Last summer a commission went to Trinidad to study the malarial situation in the vicinity of the large army base that is being established. It was demonstrated that the only important vector of malaria in the area around the base was *Anopheles bellator* (De Verteuil, 1935; Rozeboom, Fox, and Laird, 1941). This mosquito breeds in collections of water at the bases of the bromeliads, that grow as parasites on the immortelle trees. These trees were planted in great numbers in the early days to shade the cacao groves. The cutting down of the immortelle trees in the vicinity of the army base

gives promise of a complete solution of its malarial problem.

Construction projects sometimes have entirely unexpected results in producing conditions favorable for the spread of malaria. The depressions, or so-called "borrow pits," made by the removal of dirt for the fills in road construction, are in many parts of the South important breeding places for malaria-transmitting mosquitoes. The impounding of water in hydraulic power projects frequently leads to the spread of malaria by producing ecological relations particularly favorable for the breeding of anopheline vectors. In a mining town in the foothills of the Sierras in California pools of water caused by leakage from a dam produced malaria over a period of years in a considerable proportion of all the people. Arrangements for proper drainage soon completely remedied this situation. Also, the Tennessee Valley Authority has found it necessary to organize a large research staff of malariologists to investigate and combat the conditions favorable for the spread of malaria brought about by changes in water levels produced by its dams.

Sometimes in highly civilized communities there may be carelessness in the handling of the complicated machinery of public utilities. Whole water supplies may be invaded by disease-producing organisms or defects may develop in the systems for the disposal of human wastes. A striking example of a situation of this type produced the epidemic of amebic dysentery that occurred in Chicago in 1933 during the World's Fair. Here, defects in the plumbing system caused the introduction of sewage into the drinking water supplies of two hotels and produced such concentrations of the amebic cysts that large numbers of people contracted severe cases of dysentery. (See Bull. 166 of the National Institute of Health).

An important cause of the acquisition of new parasites by man has been his domestication of animals. Several parasites of dogs and cats have become adapted to live in

the human host. Trichinosis, a nematode disease of pigs and rats, has become common in man from his domestication of the pig for food. Since other animals rarely eat human flesh, man is a "blind alley" host and his infection is of no advantage to this parasite. In the United States it has been found that human infection depends largely on the feeding to pigs of garbage containing raw pork scraps. Trichinosis can be controlled either by reducing the consumption of raw or imperfectly cooked pork or by regulations against the feeding of uncooked garbage to pigs.

The methods of animal husbandry used in sheep raising in Iceland, Australia, the Argentine and certain other countries have produced wide-spread human infection with hydatids, the larval stage of the dog tapeworm, *Echinococcus granulosus*. In such regions the normal cycle of this parasite involves dogs and sheep. Eggs from the adult tapeworms in the dogs which tend the sheep contaminate the pastures and are ingested by the sheep. In this host large cysts, each containing thousands of the tapeworm heads, grow in the liver and other organs. The dogs are infected when they feed upon the viscera of the infected sheep on the range or are allowed to eat the offal from slaughter houses. Man in this case, also, has no part in the normal life cycle of the parasite; but whenever he ingests the eggs passed by dogs harboring this tapeworm, the large hydatid cysts, which cause severe disease and frequently death, develop in his organs. In such associations man can reduce his danger of infection by keeping the dogs from eating the carcasses of sheep and by care in his relations with the dogs.

Many examples of human factors that are favorable in parasite ecology are found in a wide variety of agricultural practices. Irrigation often aids in the spread of malaria and filariasis by increasing the breeding places of the mosquito vectors. The use of human excrement as fertilizer as practiced in the Orient is an important factor in the spread of intestinal parasites. A rather unusual

example of this relation occurs in China, where there is an association between sericulture and hookworm disease. Field studies in a rural silk-producing district near Soochow (Cort *et al.*, 1926) showed almost ideal conditions for the spread of hookworm infection produced by the methods used in the cultivation of mulberry trees. After the first picking of the mulberry leaves in April or early May to feed the spring brood of silkworms the farmers commonly fertilize the trees with night soil (diluted human excrement) to force the rapid growth of more leaves. The liquid fertilizer is poured around the bases of the trees usually in late May or early June after the soil has been turned over and thoroughly broken up. The second picking of the mulberry leaves comes about two to four weeks later. By this time, any viable hookworm eggs that were present in the night soil poured around the trees have developed into infective larvae. The methods of picking the leaves give ample opportunity for hookworm larvae to penetrate into the feet of the pickers, and inquiries elicited the information that most of the ground itch, the condition produced by penetration of the larvae, was acquired at this time. These reports and the repeated finding of large numbers of infective hookworm larvae on the surface of the soil around the trees indicated that most of the hookworm infection in this region was acquired in this way. In fact, no other sources of infection of any significance were found. In this situation, therefore, severe hookworm disease is acquired by contact for a very limited time with specific sources of infection set up by a single phase in the complicated practice of sericulture. The farmers themselves recognized the relation of the disease which they called "mulberry leaf yellow" to the second picking of the mulberry leaves. They stated that the ground itch in the feet, which they attributed to the entrance of evil spirits, was followed in a few days by a cough and after a few weeks by pallor and weakness. The only link in the chain they had missed was

the relation of the night soil used in fertilizing the trees to the infection.

Simple and effective control procedures can be suggested. Only when the night soil used in fertilizing the trees contains numbers of viable hookworm eggs, will there be a chance for appreciable infection. Most dangerous, therefore, is the use by the farmers of comparatively fresh fertilizer from their own storage pits. Hookworm eggs die in a short time in stored night soil, especially when it is mixed with urine, lime or other fertilizers. Also, night soil purchased from nearby cities would be almost entirely free from hookworm eggs, since in such populations there is practically no hookworm infection. It can be seen, therefore, that only minor changes in the methods of fertilizing the mulberry groves would serve to eliminate the sources of infection. Some day, when conditions become more settled in China, the application of these simple control procedures will save millions of people from hookworm disease in the silk-producing regions and will raise the level of health of whole populations.

Another agricultural practice that has been found to be particularly favorable for the spread of hookworms is the picking of coffee in Puerto Rico (Cort, Riley and Payne, 1923). Here, the coffee trees are grown in deeply shaded groves covering much of the hill country. The warm, moist, humus soil of these groves offers ideal conditions for the development of hookworm larvae. As soon as the coffee berries begin to ripen in the late summer the pickers go into the groves in small groups for the first round of picking. Two weeks later, a somewhat larger group makes the rounds, and this continues at intervals of two weeks for the three or four months of the coffee-picking season. At the height of the season several hundred pickers may be working on one estate. At each round every tree on the whole estate must be reached. The bare feet of the pickers, therefore, come into contact with much of the soil surface of the grove during the

course of one round of picking. They are paid by the sac, and so often spend the whole day in the groves starting with the first light and remaining until it is too dark to see. This means that as they work through the groves they spread their stools widely. By the next round nests of infective hookworm larvae will have had ample time to develop where each infected stool was deposited. As the picking season progresses, therefore, centers of infested soil will become increasingly numerous and wide-spread and contact with them will become increasingly frequent. The height of the coffee-picking season coincides with the period of heaviest rains, so that the pickers often work under conditions where the feet and legs become covered with mud. This gives any infective larvae in the soil a particularly favorable opportunity to penetrate. At times after an unusually wet day at the height of the picking season, half of the workers on an estate will be entirely incapacitated from the ground itch produced by the penetration of the hookworm larvae. It is not surprising, therefore, that the worst centers of hookworm disease in Puerto Rico are found in the hill country where coffee is grown and that the worst cases are among the coffee pickers.

The diseases caused by the human blood flukes, the schistosomes, also, offer striking examples of man-made conditions associated with agricultural practices that are favorable for parasite dissemination. After the eggs of these trematodes pass from the human body they hatch almost immediately and the miracidia swim actively in the water and penetrate into certain species of snails. In these intermediate hosts a peculiar type of reproduction takes place and large numbers of cercariae are produced. They escape into the water and infect man by penetration through the skin. Spread of the human species of schistosomes, therefore, depends on infection of the snail intermediate hosts in the water from eggs passed from man, or reservoir hosts, and the contact of man with water containing the free swimming cercariae that have escaped

from the snails. Therefore, any factors that tend to bring these hosts into close relationship with each other will serve to increase human infection.

Over much of the extensive areas where the three species of human schistosomes are endemic the relation of man and the snail intermediate hosts is rather casual; and schistosomiasis occurs in small, widely scattered foci, usually with a low incidence. However, in China, especially in the Yangste Valley, and in Egypt, in the delta and valley of the Nile, this disease is extraordinarily widespread and intense and affects millions of people, causing great morbidity and mortality. Epidemiologic studies of recent years have demonstrated that in these huge endemic areas the disease is man-made, and is of such great importance because of agricultural practices particularly favorable for its spread.

In China the oriental type of schistosomiasis is largely an occupational disease of farmers who cultivate rice by the wet method (Faust and Meleney, 1924). In the cultivation of this crop very favorable ecological conditions for the snail intermediate hosts are produced, especially in the numerous irrigation canals used in bringing the water to the rice fields and in draining them. Infection of the snails is made easy by the use of human excrement in fertilizing the fields and by the wide-spread use of water buffaloes (Wu, 1938) in preparing the fields, since this animal is an important and frequently infected reservoir host. Opportunity for human infection is abundantly produced by the working of the farmers for long periods of time barelegged in the irrigation ditches and in the rice paddies, where a limited amount of water makes possible great concentration of the cercariae. So here, age-old agricultural practices in the cultivation of China's most important food crop produce conditions so favorable in this parasite's ecology that tens of millions of people are infected and hundreds of thousands die each year.

In Egypt, schistosomiasis, or bilharziasis, as it is fre-

quently called is extremely prevalent. It has been estimated that at least 7,000,000 of the 12,000,000 people living in the rural districts are infected with either or both of two species of blood flukes (Scott, 1937a). Severe cases are common and the death rate is high. Here, as in China, the situation is man-made. The system of perennial irrigation that is used over most of Egypt brings man and the snail intermediate hosts together under conditions almost ideal for the spread of these parasites. By the control of the flow of the Nile with huge dams and by an extensive system of canals the waters of this mighty river are spread over the cultivated lands. Almost the whole country is covered with an intricate network of canal systems. The small terminal distributing canals border almost every field and the water is carried away by innumerable drainage canals. Wherever the water in these smaller canals is slow-moving, masses of vegetation grow and in such habitats millions of the snails in which the blood flukes develop find an environment favorable for their life. Sanitary facilities are almost entirely lacking and the people defecate and urinate freely in the canals and along their banks, giving abundant opportunity for the infection of the snails. The whole population spends much time in the waters of these canals, in the play of the children, in the washing of clothes and other activities of the women and in the work of the men in the fields. The result of this close relation between the snails and man is the production of the most concentrated endemic center of schistosomiasis found anywhere in the world.

Contrasted with the favorableness of perennial irrigation for the spread of these parasites is the situation found in those few areas in Upper Egypt where irrigation is simply a matter of flooding the fields at the time of high water in the Nile. Here suitable habitats for the snail hosts are comparatively few and the incidence of schistosomiasis is low. It is known from examinations of mummies that this disease was present at the time of the Pharaohs. All the evidence indicates, however, that it

was not until the wide-spread development of perennial irrigation in modern times that it became a real menace.

Modern irrigation engineering has tremendously increased the productivity of Egypt so that its population has increased to the saturation point. It has not, however, been a blessing to the people on the land because it has inflicted on them a scourge the extent of which makes the plagues inflicted on the ancient Egyptians by Moses seem insignificant. It has been estimated that when new lands in Egypt are brought under perennial irrigation each increase of $8.00 per year in the value of crops raised will make it possible for one more Egyptian to live. The present government program calls for the bringing of 700,000 more acres under perennial irrigation in the next decade. The conclusion seems almost inescapable that this "improvement" will doom another 1,000,000 people to infection with schistosomiasis (Scott, 1937b). Intensive investigations are in progress to discover control methods. The most promising center around attempts to modify the canals so that they will be unsuitable as habitats for the dangerous snails. The whole control program, however, is still in an entirely experimental stage, and it looks as if the rural population of Egypt would continue to suffer for many years to come from the effects of the introduction of a modern system of irrigation.

Schistosomes also have human relations in the United States. The cercariae of several species of blood flukes of small mammals and water birds which develop in a number of species of snail intermediate hosts will penetrate the human skin and produce a severe dermatitis (Cort, 1928). The parasites in the skin of man are quickly destroyed by the hosts's defenses, and there is not the slightest evidence that they can reach the blood stream and develop further. In fact, the severity of the skin reaction which causes an intense itching seems to be produced because the cercariae have penetrated into an unsuitable, that is, an abnormal host. The prevalence of

the "schistosome dermatitis" produced by the cercariae of these blood flukes is associated with certain specific human factors. Near the University of Michigan Biological Station several species of schistosome cercariae which can penetrate the human skin live in lymnaeid snails whose usual habitats are muddy pools or swampy areas. They produce an occupational disease of biologists's "collectors' itch," for other inhabitants of the region will not usually visit such places. Biologists may avoid the ravages of this disease by wearing hip boots, and by using nets rather than their hands for collecting purposes.

In addition, in northern Michigan and elsewhere in the lake regions of our central states and Canada, schistosome dermatitis is frequently associated with summer vacationing (Cort, 1936). This type of the disease or "swimmers' itch," as it is frequently called is produced by cercariae that develop in snails that inhabit beaches suitable for bathing purposes. These parasites penetrate in numbers the skin of bathers who on warm summer days loll or play in the shallow water of the beaches near the shore. It is interesting to note that the human factors that produce schistosome dermatitis are unfavorable both to man and to the parasites. Man scratches desperately to relieve the itching and the parasites are killed in the skin of the abnormal host and thus fail to complete their normal life cycle.

From the examples that have been given it is apparent that human factors in parasite ecology are extraordinarily numerous and variable. They may work to the advantage of man and the disadvantage of the parasites. Most significant of such factors are those that come from conscious human effort directed toward the destruction and control of the parasites. On the other hand, we have seen that those human factors in parasite ecology that are favorable to the parasites and, therefore, disadvantageous to man, run the whole gamut from simple individual habits to the most complicated group activities. It is the

increasing knowledge of such factors and just how they work to the advantage of the parasite that is laying the scientific foundations on which adequate control procedures are being gradually built.

LITERATURE CITED

Clark, H. C.
1928. *Am. Jour. Trop. Med.*, 18: 1, 1–7.
Cort, W. W.
1928. *Jour. Am. Med. Assn.*, 90: 1027–1029.
1936. *Am. Jour. Hyg.*, 24: 2, 318–333.
Cort, W. W., W. A. Riley and G. C. Payne
1923. *Am. Jour. Hyg.*, 3 (July Suppl.): 111–127.
Cort, *et al.*
1926. *Am. Jour. Hyg.*, Mono. Ser. No. 7, 188–222.
De Verteuil, E. J.
1935. Administration report for the Surgeon General for the year 1934. Govt. Printing Office, Port-of-Spain, Trinidad.
Faust, E. C., and H. E. Meleney
1924. *Am. Jour. Hyg.*, Mono. Ser., No. 3: 1–339.
Moorthy, V. N., and W. C. Sweet
1936. *Indian Med. Gaz.*, 71: 10, 565–568.
Rozeboom, L. E., L. A. Fox and R. L. Laird
1941. *Science*, 94: 2431, 114.
Scott, J. A.
1937a. *Am. Jour. Hyg.*, 25: 3, 566–614.
1937b. *Jour. Trop. Med. and Hyg.*, 40: 11, 125–132.
Stitt, E. R.
1928. *U. S. Naval Med. Bull.*, 26: 4, 801–817.
Wu, Kuang
1938. *Am. Jour. Hyg.*, 27: 2, 290–297.

HUMAN GENETICS[1]

THE MUTANT GENE IN MAN

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THE rapidly developing knowledge of human heredity has resulted, among other things, in the formulation of practical applications of this knowledge to the welfare of mankind (*cf.* Macklin, 1941; Snyder, 1940, 1941; Wiener, 1941). The practical applications include those in medicine (diagnosis and prevention), in courts of law (paternity proceedings, exchanged infants, inheritance cases, rape and divorce actions) and in genetic prognosis (advice in prospective marriages and prospective pregnancies).

Before a genetic trait in man may be used in one or another of these practical applications, certain basic facts about the mutant gene responsible for the trait must be ascertained. It seems worth while at this stage of the development of human genetics to pause and summarize the various relationships of the mutant gene in man. Knowledge of some of these is quite necessary, and knowledge of all of them is desirable, before setting up practical applications in regard to the trait conditioned by any gene. We may classify the basic relations of the mutant gene in man under four main headings: spatial relations, physiological relations, ontogenetic relations, and phylogenetic relations (Table 1).

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TABLE 1

THE MUTANT GENE IN MAN

I. Spatial relations
  A. Absolute location
    1. On an autosome (autosomal)
    2. On the non-homologous portion of the X-chromosome (sex-linked)
    3. On the non-homologous portion of the Y-chromosome (Y-borne)
    4. On the homologous portions of the X- and Y-chromosomes (incompletely sex-linked)
  B. Relative location with respect to any other gene not an allele
    1. On a chromosome of another pair (independent)
    2. On a chromosome of the same pair (linked)
      a. On the same chromosome of the same pair in any given individual
      b. On the other chromosome of the same pair in any given individual
II. Physiological relations
  A. Penetrance
    1. Similar in both sexes
      a. Complete
      b. Reduced
    2. Different in the two sexes
    3. Restricted to one sex (sex-limited)
  B. Expressivity
    1. Similar in both sexes
      a. Constant
      b. Variable
    2. Different in the two sexes
  C. Viability produced in an individual having the gene
    1. Similar in both sexes
      a. Complete
      b. Reduced
      c. Eliminated (lethal)
    2. Different in the two sexes
III. Ontogenetic relations
  A. With respect to its own allele
    1. Dominant
    2. Recessive
    3. Intermediate
    4. Dominant in one sex, recessive in the other (sex-influenced)
  B. With respect to any other pair of alleles
    1. Epistatic
    2. Hypostatic
    3. Additive
    4. Multiplicative
    5. Indifferent
IV. Phylogenetic relations
  A. Frequencies of the gene and its alleles
    1. Constant
      a. With genotypic equilibrium (under a system of random mating)
      b. Without genotypic equilibrium (if the lack of equilibrium is due to assortative mating)
    2. Changing
      a. Due to mutation pressure
      b. Due to selection pressure
      c. Due to scattering of the variability
      d. Due to combinations of a, b and c
  B. Frequencies of the genotypes formed by a gene and its alleles
    1. Constant (in equilibrium)
    2. Changing (not in equilibrium)
      a. Due to changing frequencies of the gene and its alleles
      b. Due to assortative mating
      c. Due to migration

Taking these up in order we may logically ask about the spatial relations of a gene. We first inquire as to its absolute location. It may be autosomal, located on one of the twenty-three pairs of autosomes, and giving no evidence of association with the sex chromosomes. This type of hereditary behavior is so well known as to require no further comment. The number of reasonably well-established autosomal loci in man now runs well into the hundreds.

A gene may, however, be associated with the sex chromosomes, in which case there are three possibilities. It may be sex-linked, it may be Y-borne, or it may be incompletely sex-linked.

With the discovery by Koller and Darlington of distinct histological portions of the sex chromosomes of mammals, it became apparent that genes associated with the sex chromosomes might conceivably be on any one of these portions. The regions are as follows: first, a portion of the X-chromosome homologous with a corresponding portion of the Y-chromosome, the two portions showing chiasmata in meiosis; second, a portion of the X-chromosome non-homologous with any part of the Y-chromosome; and third, a portion of the Y-chromosome non-homologous with any part of the X-chromosome. The non-homologous portions are, of course, non-pairing in meiosis.

In man, genes have been located on each of these three portions. Those carried on the non-homologous part of the X-chromosome are spoken of as sex-linked, and their behavior is familiar to all of us. Upwards of thirty such genes are known in man, variously affecting the eyes, the skin, the muscles, the nerves, the glands and the blood.

Genes carried on the non-homologous portion of the Y-chromosome are spoken of as Y-borne or holandric. The transmission will be from an affected father to all his sons, and the condition does not occur in women. The four known Y-borne mutations in man result in the following traits.

Ichthyosis hystrix gravior, described by Maschin in 1732, has been handed down in typical fashion for six generations. At the end of two weeks the affected individuals begin to develop a dark thick rugged bark-like skin on the whole body with the exception of the face, palms and soles.

One form of webbed toes, described by Schofield in 1912, involving the second and third toes, has been transmitted as a Y-borne gene for four generations. Keratoma dissipatum, described by Brauer in 1913, has been found in two separate families. It involves small, hard, non-painful lesions on the hands and feet. Hypertrichosis of the ears, described by Tommasi in 1907, is a striking and curious condition in which a dense growth of long hair develops on the ears. Eleven males in five generations have received the gene for this trait on the Y-chromosome from their affected fathers.

The third kind of hereditary transmission associated with the sex chromosomes involves genes located on the homologous portions of the X- and Y-chromosomes. Such transmission is known as incomplete sex-linkage. The search for genes of this sort has resulted in the discovery of six of them by Haldane. Such genes behave as ordinary autosomal factors except for one thing: some families will contain more affected males and unaffected females than would be expected on the basis of autosomal inheritance, while others will contain more affected females and unaffected males. If the gene concerned is dominant, the affected offspring of affected fathers will tend to be of the same sex as the paternal parent from whom the father received the gene. If the gene concerned is recessive, the situation is less obvious and the requisite statistical analysis is intricate.

Because of the fact that the genes located on the homologous portions of the sex chromosomes will appear to be autosomal unless carefully studied with special technics, it is important that all newly described genes be analyzed from this standpoint. I have recently com-

pleted an analysis of four sets of alleles in man, dealing with blood groups, blood types and two kinds of taste deficiency, which indicates that no one of these sets is incompletely sex-linked.

The six known incompletely sex-linked genes are as follows. Total colorblindness is a rare condition involving nystagmus, photophobia and amblyopia, resulting in vision in which the world appears in shades of gray or in black and white. Xeroderma pigmentosum is an abnormal sensitivity of the skin to light, involving increasing freckling and reddening of the skin, followed frequently by malignancy and death. Oguchi's disease is a form of night-blindness in which a diagnostic criterion is the golden appearance of the light-adapted fundus upon ophthalmoscopic examination.

The recessive type of epidermolysis bullosa is a severe, malignant form of skin blisters, in which the bullae are between the epidermis and the corium and leave permanent scars. It is usually fatal in infancy or childhood.

The genes for two forms of retinitis pigmentosa are also found on the homologous portions of the sex chromosomes. The two genes are alleles, one being dominant and the other recessive to the normal condition.

We have seen in the foregoing discussion that a mutant gene in man may be found to have its absolute location in one of four general regions of the chromosomes. Next we may inquire as to the relative location of a gene with respect to any other gene not an allele. Here the gene may be on a chromosome of another pair, in which case we consider it independent of the second gene. On the other hand, it may be on a chromosome of the same pair, in which case it is linked to the second gene.

The low frequency of many mutant genes in the human population means that we are seldom able to study crossing over between any two of them, because we so seldom find two traits determined by known mutant genes in the same family. Moreover the classic experimental analyses of linkage are not available to us in human beings.

Nevertheless much progress has been made of late years in the direction of chromosome mapping in man.

It will at once be realized that the twenty-odd sex-linked factors must be linked. Since they are so very rare, however, practically no crossing-over studies have been made on them. In the case of the incompletely sex-linked genes, on the other hand, crossing-over can always be studied between such a gene and sex, or, to express it more precisely, between the gene and the unpaired non-homologous portions of the X- and Y-chromosomes. This is not the time nor the place to discuss the technics involved, but the elaboration and use of such technics by Haldane has resulted in the mapping of the homologous portions of the sex chromosomes for the six known incompletely sex-linked genes.

In the case of autosomal genes the difficulties are still greater. Technics of ever-increasing efficiency are being developed, however, and are being used on those mutant genes the frequency of which in the population is reasonably large. I have recently discussed elsewhere the development and use of such technics (Snyder, Baxter and Knisely, 1941) and will merely mention in passing that their employment by a number of workers has resulted in evidence for the independent transmission of the genes for the blood groups, the blood types, the taste deficiency to P.T.C., eye color, allergic disease, recessive polydactylism and telangiectasis.

Penrose (1935) found indications of linkage between the genes for the blood groups and red hair. Burks (1937) has presented evidence for the linkage of the genes for hair color and the congenital absence of certain teeth, and for eye color and myopia. My colleague, Dr. Rife, has recently reported linkage between handedness and an interdigital palm pattern (1941). Mr. Kloepfer, a student in my laboratory, has just completed an analysis of 153 tests for linkage involving 17 different traits. Twelve of the 153 tests give evidence for linkage of the genes concerned. These results will be published in the near future.

Thus the mapping of human chromosomes is rapidly becoming a reality, and we may properly inquire penetratingly into the spatial relations of the mutant gene.

Second, we may investigate the physiological relations of the gene. Here I include the penetrance of the gene, its expressivity and the viability produced in an individual possessing the gene. Penetrance is essentially an all-or-none phenomenon. In man, it is usually spoken of in connection with dominant genes, although it may very well be found to apply to recessive genes as well. If a dominant gene always produces its effect in an individual possessing the gene, it is said to have complete penetrance. If, however, some persons possessing the gene do not show the trait, the gene is said to have reduced penetrance. Ideally the degree of penetrance should be stated for each gene.

The differentiation between a dominant gene with low penetrance and a recessive gene can be accomplished only with large and unbiased samples. It is done by comparing the proportions of affected sibs, parents, offspring and other relatives of affected propositi. The rationale of penetrance is the residual heredity on the one hand and the environment on the other. Obviously much practical work remains to be done in this connection.

The penetrance of human genes varies from a fraction of a per cent. in leukemia, through about 10 per cent. in diabetes mellitus to complete or nearly complete expression in such traits as the blood groups. The recent work of Lennox and his coworkers on epilepsy and cerebral dysrythmia provides an excellent attack on problems of penetrance. Studies of epilepsy have indicated the possibility that a dominant factor with reduced penetrance might be a possible explanation. Electroencephalograph studies of epileptic patients and their relatives indicate that many of the relatives show the same cerebral dysrythmia shown by epileptics, without actually having epilepsy themselves. It may be possible to measure the penetrance of the gene for epilepsy more accurately by means of the electroencephalograph.

Penetrance may be similar in both sexes, or differentially reduced, as in the Laurence-Moon-Biedl syndrome. When it is eliminated in one sex, the gene is said to be sex-limited.

In addition to penetrance, we speak of the expressivity of a gene. The term is self-explanatory, indicating the variability in the trait produced by the gene. The blood group genes have rather constant expressivity, producing only restricted variations in sensitivity or titre. The gene for minor brachydactyly shows more variable expressivity, ranging from the production of extremely short phalanges of the index fingers and second toes to a shortening recognizable only by careful comparative measurement. The gene for hemolytic icterus shows considerable variation in expressivity, the trait varying from severe clinical anemia and jaundice to preclinical or laboratory signs such as microcytosis, increased fragility and reticulocytosis.

Neurofibromatosis, or von Recklinghausen's disease, presents a striking example of variable expressivity. The disease involves skin lesions and lesions of the peripheral nerves. The condition is due to a dominant gene which at first was thought to have low penetrance. More careful studies indicate that the penetrance is very high, but the expressivity is variable, including café-au-lait spots, pachydermatocoeles, plexiform neuroma, fibroma molluscum, subcutaneous tumors and elephantiasis neuromatosa.

As in the case of penetrance, expressivity may depend upon the residual heredity (modifying factors) or upon variations in the environment. Again there is need for practical research in this direction.

Among the physiological relations of the gene is the viability which it produces in individuals possessing the gene. Viability may be high, or reduced. It may even be eliminated at an early stage of development, in which case we speak of the gene as lethal.

The third set of genic relations to be investigated I have called ontogenetic relations. We may inquire into

such relations of a mutant gene first with respect to its own allele. Here the gene may be dominant, recessive or intermediate. It may be dominant in one sex, recessive in the other, in which case we refer to it as sex-influenced.

With respect to any other allele the gene may be epistatic, hypostatic or indifferent. It may be directly additive with a constant absolute effect, or multiplicative. These ontogenetic relations of the gene are so well known that they need no discussion and we may pass directly to a specific application of these relations to medical genetics.

In man, autosomal dominant, autosomal recessive and sex-linked transmission often occur within what appears to be the same clinical entity. These may sometimes be broken up into more or less distinct clinical conditions after the genetic evidence is available. For example, there is a dominant and a recessive form of epidermolysis bullosa dystrophica. While superficially similar, the dominant form does not affect the teeth nor hair, but thickens and distorts the nails and results in epidermal cysts. It is not generally fatal. The recessive form results in abnormal and deficient teeth, affected conjunctiva and cornea, and the occurrence of bullae in the mucous membranes as well as in the more usual places. It is frequently fatal. Here the differentiation into clinical entities is not difficult.

In peroneal atrophy, the dominant form shows an onset in the second decade, and the affected individuals become life-long cripples. The recessive form usually shows an onset in the first decade, and is more severe, sometimes resulting in early death. Here the clinical differentiation is more difficult. In many eye defects and skin abnormalities, such clinical differentiation proves difficult or impossible even though more than one type of transmission is clearly shown in different families.

It therefore becomes necessary in giving advice to families or to prospective families to know not only the diagnosis but also the family history of the specific patient,

so as to determine the ontogenetic relations of the mutant gene concerned and thus the genetic prognosis.

On the other hand, what appear to be separate and distinct clinical entities may give genetic evidence of being fundamentally the same after all, that is variations in expressivity of the same gene or gene constellation. For example, Ardashnikov has shown that lymphatic and myelogenous leukemia appear indiscriminately within the same pedigree, a fact which may prove of importance in pathology.

Next we may inquire into a set of relations of the mutant gene which I have called phylogenetic relations. These include the frequencies of a gene and its allele, and the frequencies of the genotypes formed by a gene and its allele.

In evaluating the type of hereditary transmission involved in a human trait, particularly in determining the ontogenetic relations of the mutant gene concerned, we are frequently faced with the necessity of knowing what proportion of individuals showing the effect of the dominant gene is homozygous and what proportion is heterozygous. This in turn will depend upon the relative proportions of the dominant and the recessive gene of the pair in the population. Thus we are concerned with the frequency of a mutant gene in relation to that of its normal allele.

Consider a pair of genes *A* and *a*. Most of the genes of the population at this locus may be *A* genes, with *a* genes making up only a small fraction of the total. Or it may be the other way around, so that *a* alleles make up a large proportion of the genes at this locus. If 60 per cent. of the alleles of this set are *A* alleles, and 40 per cent. are *a* alleles, we say that the frequency of *A* is 0.6, and the frequency of *a* is 0.4. By means of special technics it is possible to calculate the frequency of a mutant gene with respect to its own allele and with respect to another gene not an allele, and then to use these calculations in determining whether the mutant gene is dominant, recessive, epistatic or otherwise. I have discussed

the history and development of such technics at some length in other places (Snyder, 1934 a, b; Snyder and Cotterman, 1936; Snyder and Yingling, 1935; Cotterman and Snyder, 1937, 1939, etc.) and the paper of Dr. Cotterman to follow will elaborate on this point.

The frequency of a mutant gene may vary from 0 to 1, these being only limiting values. Moreover, this frequency may remain the same from generation to generation, or it may change. The system of mating will not change it, as long as each individual has an equal opportunity to reproduce. Thus the gene frequency may remain constant either with random or with assortative mating, although the relative frequencies of the genotypes formed will differ in the two conditions. Before looking into this let us inquire into the conditions under which the gene frequencies *will* change from generation to generation. These conditions include mutation pressure, selection pressure and the scattering of the variability.

As Dobzhansky has pointed out, the accumulation of germinal changes in a population is, in the long run, essential to the evolutionary plasticity of the species. Mutation pressure provides this accumulation of change, and even unfavorable recessive mutations may produce an increase of variability, since the mutant gene can increase by random variation at least until the heterozygotes become so frequent in the population that they are likely to mate, and the homozygote is produced. Mutations are frequently reversible, and the net effect of mutation will depend upon the equilibrium reached as a result of the two opposing mutation rates.

Mutation rates have been calculated for only two genes in man: hemophilia, a sex-linked recessive factor, and epiloia, an autosomal dominant factor. The mutation rates appear to be about the order of one in 100,000.

Selection pressure combined with mutation pressure may cause rapid changes in the gene frequencies and thus in the composition of a population if mutation to an allele favored by selection occurs more frequently than the

reverse mutation. Conversely, selection may act very slowly indeed if the net mutation rate is towards an allele opposed by selection. Complete analyses of the theoretical effects of mutation pressure and selection pressure have been presented by Wright (1931, 1932), Fisher (1932) and Haldane (1932).

Mutant genes may change in frequency in a population, and may even become lost, without regard to mutation pressure or selection pressure, through a process inherent in the very mechanism of Mendelian heredity: a process called by Dobzhansky the scattering of the variability. Even mutations favored by selection may become lost in small breeding populations through random variations in the frequencies of the genes. Here the size of the breeding population becomes important, since in very large populations the scattering of the variability becomes relatively ineffective, while in small isolated populations this process may even transcend mutation rates.

An example of the confusion caused by a lack of understanding of the possibilities inherent in the scattering of the variability is presented by some of the earlier criticisms of the anthropological aspects of the blood group distributions (Schütz and Wöhlisch, 1924; Lanner, 1925; Grove, 1926). Here the validity of the results from the population standpoint was questioned on the basis of observations that the range of variation between small isolated villages in the same general locality was sometimes greater than that between so-called racial groups. This variation is just what must be expected under conditions involving small isolated breeding populations.

With changes in the frequencies of alleles will come parallel changes in the frequencies of the genotypes formed by the combination of the alleles. Referring to our pair of alleles *A* and *a*, the three genotypes formed by their combination will be *AA*, *Aa* and *aa*. The relative frequencies of these three genotypes in the population may remain constant from generation to generation, or they may change. A population in which the frequen-

cies of the genotypes remain constant is said to be in equilibrium. The equilibrium ratio is, as was first pointed out by Hardy (1908), a binomial one. That is, a population is in equilibrium when the frequencies of the genotypes *AA*, *Aa* and *aa* are proportional to the ratio $p^2 : 2pq : q^2$, where p is the frequency of the gene *A*, q the frequency of the gene *a*, and $p + q = 1$.

Only where dominance is lacking, and all three genotypes are phenotypically distinguishable, can the equilibrium ratio be directly tested. In the case of dominance, where two of the three genotypes are indistinguishable, there is no direct way to test it. It can be indirectly tested, however, by investigating the occurrence of random mating, since the equilibrium distribution will be established for a single pair of alleles in a single generation under a system of random mating with respect to the contrasting characters.

Changes in the frequencies of genotypes can be caused by two phenomena in addition to mutation, selection and scattering of the variability. One of these is assortative mating. Unlike the three just mentioned, however, it affects directly the frequencies of the genotypes, and does not change the frequencies of the genes concerned. The other phenomenon is migration, which may subsequently affect the gene frequencies as well.

The concept of equilibrium leads directly to an obvious practical conclusion, but one which is frequently overlooked in discussions of human genetics, particularly medical genetics. Stated simply, in terms of a large population breeding at random, and without regard to mutation or selection, the ratio of carriers of a recessive gene to those actually showing the character determined by the gene will vary from trait to trait, depending upon the frequency of the trait (and thus of the gene) in the population. In the case of a trait which occurs in one out of a million of the population, the carriers will be about 2,000 times as frequent as those who show the trait. If the trait occurs in one out of a thousand, carriers will be sixty times as common as affected individuals. If it

occurs in one out of a hundred, they will be only eighteen times as common as affected persons. For a trait occurring in one out of six, there will be but three carriers to every affected person, and so on. Recognition of this fundamental principle would obviate many unnecessary controversies in medical genetics.

If the occurrence of the equilibrium ratio can be established in regard to a pair of contrasting characters, we may proceed to the determination of the frequencies of the genes concerned, as was outlined previously. The practical results of such determinations in human biology are of two sorts. First, such information is, or at least should be, the basis for the study of human ecology, where the investigations must center around the distributions of genes, not of phenotypes. This point is the subject of Dr. Strandskov's paper, which follows. Second, the gene frequencies are of major importance in the establishment of the ontogenetic relations of the particular mutant gene concerned.

An understanding of the significance of the frequencies of genes and genotypes would go far towards eliminating from the literature such incorrect statements as the following: "Albinism is a recessive factor, which explains why it is so rare," and "Left-handedness occurs in 25 per cent. of the population, which indicates that it is a Mendelian recessive."

In this discussion I have tried to classify and clarify the various relations of the mutant gene in man which are of importance in an understanding of human heredity, and which are essential to the setting up of practical applications of this study in prognosis, diagnosis, prevention and forensic affairs. Now and then I am told by some younger geneticist that he would like to enter the field of human heredity, but that he hesitates to abandon experimental work and fears that he may be embarking on non-scientific procedures. I trust that it will be realized that the study of human heredity can be not only scientific but to a certain extent experimental, and that such study forms a legitimate branch of the science of genetics.

LITERATURE CITED

Burks, B. S.
1937. Yearbook, Carnegie Inst. of Wash., 36: 312.

Cotterman, C. W. and L. H. Snyder
1937. *Genetica,* 29: 237.
1939. *Jour. Amer. Statistical Assn.,* 34: 511.

Dobzhansky, Th.
1941. "Genetics and the Origin of Species." New York: Columbia University Press.

Fisher, R. A.
1932. *Proc. Sixth Internat. Cong. Genetics,* 1: 165.

Grove, E. F.
1926. *Jour. Immunol.,* 12: 251.

Haldane, J. B. S.
1932. "The Causes of Evolution." New York: Harper and Bros.
1935. *Jour. Genetics,* 31: 317.
1936. *Ann. Eugenics,* 7: 28.

Hardy, G. H.
1908. *Science,* 28: 49.

Koller, P. C. and C. D. Darlington
1934. *Jour. Genetics,* 29: 159.

Lanner, F.
1925. *Klin. Wochenschr.,* 4: 1477.

Lennox, W. G., E. L. Gibbs and F. A. Gibbs
1940. *Arch. Neurol. and Psychiat.,* 44: 1155.

Macklin, M. T.
1941. *Sci. Month.,* 52: 56.

Penrose, L. S.
1935. *Ann. Eugenics,* 6: 133.

Rife, D. C.
1941. *Science,* 94: 187.

Schütz, F. and E. Wöhlisch
1924. *Klin. Wochenschr.,* 5: 2016.

Snyder, L. H.
1934a. *Genetics,* 19: 1.
1934b. *Eug. News,* 19: 61.
1940. *Sci. Month.,* 51: 536.
1941. *Medical Genetics.* Durham: Duke University Press.

Snyder, L. H., R. C. Baxter and A. W. Knisely
1941. *Jour. Heredity,* 32: 22.

Snyder, L. H. and C. W. Cotterman
1936. *Genetics,* 21: 79.

Snyder, L. H. and H. C. Yingling
1935. *Human Biology,* 7: 608.

Wiener, A. S.
1941. *Sci. Month.,* 52: 139.

Wright, S.
1931. *Genetics,* 16: 97.
1932. *Proc. Sixth Internat. Cong. Genetics,* 1: 356.

THE BIOMETRICAL APPROACH IN HUMAN GENETICS

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So far the study of human heredity has made it seem unlikely that genetic processes peculiar to the human species will be discovered. Even the kinds of hereditary variations observed in man find close parallels in the genetics of other mammals. Perhaps the chief peculiarity of the study is the difference in methodology, which is commonly described by saying that the approach to human genetics must be a biometrical rather than an experimental approach. As Galton has said, "statistics . . . are the only tools by which an opening can be cut through the formidable thicket of difficulties that bars the path of those who pursue the Science of man."

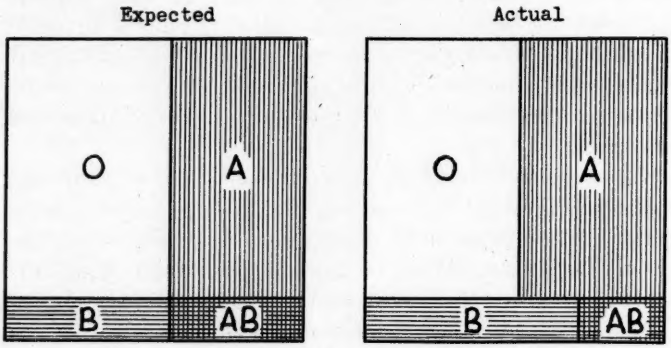
The term biometrical, however, refers more to the study of natural variability than to the use of statistical methods. Indeed, such methods are now better developed and more widely used in biology for the analysis of experiments. Their use has become so standard in genetical work that it would hardly seem appropriate to discuss a statistical approach in human genetics were it not for the fact that new and somewhat special problems arise. The studies in human inheritance which could be described as statistical are naturally very numerous and diverse. They would include the analyses of resemblance in twins, estimates of the mutation rates of certain human genes, general studies on fertility, consanguinity, the effects of maternal age, order of birth and many other topics. However, the departure in analytical method which results from the lack of experimental facilities is more clearly seen in the field of classical genetics, in the identification of single gene differences. For this reason the present review will be restricted to this branch of the subject.

The difficulties which arise here are of greater complexity, but are actually of the same kind as those encountered in experimental genetics; they concern, primarily, the inability to distinguish individuals of different genetic structure amongst individuals showing the same character. In man, the added complications arise principally from the small size of the human family and the inability to make test matings. Either of these difficulties, taken singly, would cause little trouble. In combination, however, they make necessary the use of special methods capable of detecting and measuring genetic processes in data of a more fragmentary and heterogeneous nature.

The first of three such methods to which I wish to call attention is the so-called method of gene frequency analysis. Once the mode of inheritance of a given trait has been established, these gene frequencies assume considerable interest in themselves, as Dr. Strandskov has shown. Here we shall be concerned only with their use in the initial problem of determining the kind of inheritance.

In certain situations some indication of the genetic mechanism can be inferred from data on wholly unrelated subjects, that is, from data consisting only of the frequencies of the various characters in the population. This is the situation with regard to the human blood groups, and it was Bernstein's (1925) classical statistical work in this field which first brought the attention of human geneticists to the importance of gene ratios. Bernstein showed that the then current theory of Von Dungern and Hirszfeld failed to receive support from the available data on the distribution of the four blood groups. This theory assumed the presence of agglutinogen A and agglutinogen B to be determined by separate pairs of genes (Fig. 1). If two independent pairs of genes were involved, we should expect that the proportion of individuals possessing A would be independent of the proportion possessing B. Taking the data reported by Snyder (1929) on 20,000 individuals in North

Carolina, we see that A is present in 45 per cent. of cases (adding groups A and AB), while B is present in 14 per cent. of cases (groups B and AB). In the diagram on the left, ordinates erected at these points therefore divide the square into four areas proportional to the expected frequencies in the four groups. The actual proportions, shown on the right, definitely contradict this scheme;



O - 45% A - 41% B - 10% AB - 4%

(Data of Snyder)

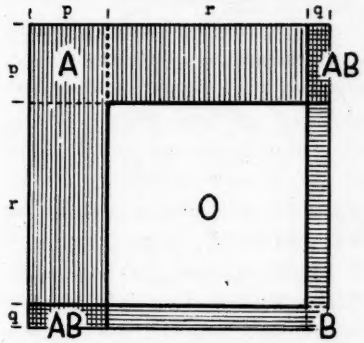
FIG. 1. Test of Von Dungern-Hirszfeld theory: two independent pairs of genes.

there are too few persons of groups O and AB and too many persons who have either agglutinogen A or B alone.

This negative correlation between the appearance of the A and B substances would suggest that the responsible genes were alternatives or alleles. So Bernstein then proceeded to test the hypothesis of three allelic genes, one for A, one for B and a third recessive gene for O. Under this scheme the frequencies of the four groups should work out as shown in Fig. 2. We first estimate from the percentages of the four groups the frequencies of the three genes, denoted by p, q and r. The expected proportions of the four groups are then computed from the gene frequencies in a manner suggested by the diagram. The actual frequencies are now so close to the ex-

pected that a separate diagram would have failed to show any visible differences. There is, however, as shown by the test of goodness of fit on the right, a slight but significant deviation in the present data. Most bodies of data, however, show reasonably good agreement with the 3-gene theory of Bernstein, and at the same time disprove the theory of two pairs of genes.

The use of gene frequencies in the analysis of family data can be illustrated by the data of Landsteiner and



	Actual	Expected*
O	9000	8961.9
A	8200	8239.5
B	2000	2049.4
AB	800	749.2

$\chi^2 = 4.99$ D.F. = 1

$P < .05$

* Computed from the maximum likelihood estimates:

(A) p = .2580 (O) r = .6694 (B) q = .0726

FIG. 2. Test of Bernstein theory: three allelic genes.

Wiener (1941) on the newly described Rh agglutinogen. By means of anti-rhesus immune guinea pig and rabbit serums, it has been demonstrated that about 85 per cent. of white persons in New York City share a certain serological property in common with the rhesus monkey. The remaining 15 per cent., lacking the agglutinogen, are designated as Rh-negative. The data analyzed by Landsteiner and Wiener consist of 60 families (Table 1). In 6 families having both parents Rh-negative, all 31 children are found to resemble the parents, suggesting that the presence of Rh may be due to a single dominant gene. To test this hypothesis further, we must examine the ratios of Rh+ and Rh– children from the two other types

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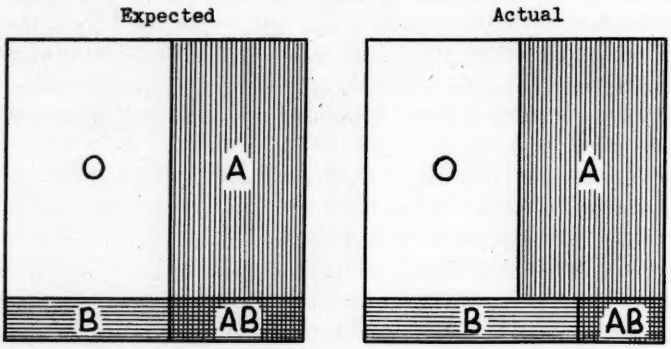

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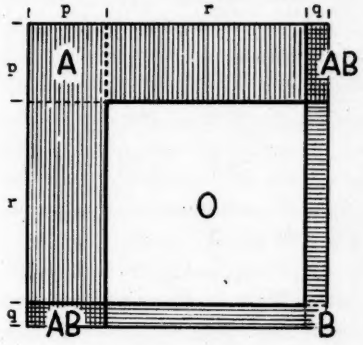

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of mating wherein one or both parents are Rh-positive. Now the peculiarity of data of this sort is seen to lie in the fact that these two classes of mating are expected to comprise mixtures of two or more genotype combinations, so that simple Mendelian ratios are not to be expected in the aggregates of the children. One procedure which can be adopted, however, consists in estimating the composition of such mixtures in terms of the gene frequencies. The

TABLE 1

INHERITANCE OF THE AGGLUTINOGEN Rh
(AFTER LANDSTEINER AND WIENER)

Mating	Number of Families	Children				χ^2
		Actual		Expected		
		Rh+	Rh−	Rh+	Rh−	
Rh− × Rh−	6	0	31	0	31	...
Rh− × Rh+	12	37	11	34.47	13.53†	0.66
Rh+ × Rh+	42	151	7	145.45	12.55‡	2.67
Totals	60	188	49			

Recessive gene frequency : $q = \sqrt{69/448} = 0.154$
$\dagger = 48 \cdot q/(1+q)$
$\ddagger = 158 \cdot [q/(1+q)]^2$

expected frequencies of Rh− children in the last two matings are found to be simple functions of the recessive gene frequency, q, and in this case are found to be reasonably close to the expected numbers. The whole of the data is therefore shown to be internally consistent and in accord with the hypothesis of a dominant gene for the Rh agglutinogen.

Methods such as those just described are based on the assumption of random mating amongst the various genotypes or phenotypes in the population. Whether such randomness occurs can of course be determined by direct observation. In the particular variations to which the gene frequency methods have thus far been applied, namely, the inherited blood differences, taste reactions, etc., the assumption appears to be well justified. Whether adjustments for assortative mating will have to be made in other cases remains to be seen.

In the study of rare pathological conditions, however, there is little or no need for gene frequency considera-

tions, because, if a gene is quite rare, almost all affected individuals will arise from one type of mating only. And since the investigations always proceed from the observation of affected individuals, no problems of mixed matings are encountered. A new and somewhat more troublesome problem, however, is created by the selective sampling. It is somewhat technical, but it deserves mention here because it illustrates one way in which the mathematical work on human heredity has been helpful, namely, by giving guidance to better methods of collecting and reporting data.

The problem is not particularly one of genetics and can perhaps be best introduced by means of an analogous problem proposed by Haldane. He says: "If I asked every child leaving school in London this year how many brothers or sisters he or she had and then calculated the average, it would be much higher than the average family size in London. First of all, I should have no representatives of childless families. Secondly, I should have ten times as big a chance of getting a child from a family of ten as from a family of one. So I should greatly exaggerate the number of large families." In a similar way, calculations on the proportions of affected brothers and sisters of patients showing any kind of hereditary defect are almost certain to give exaggerated estimates. A correction can easily be applied for the omission of families with zero affected children, but this may not be sufficient. Unless the search for families showing the particular hereditary abnormality has been exhaustive, the data are likely to be biased in favor of families showing the larger numbers of affected individuals.

Exact numerical analyses of pedigrees of hereditary defects have been very few, for which there are undoubtedly many reasons. First, the recording of pedigree data has been frequently done by workers unfamiliar with the special requirements of data to be subjected to such analysis. Secondly, the requirements themselves are perhaps none too well understood. One procedure

of recording the pedigrees and making the necessary adjustments in the ratios has been carefully elaborated by Fisher (1934). But there are other methods of securing family histories which would seem to call for different treatment. Finally, the calculation of carefully corrected ratios may have appeared to be a rather superfluous occupation. It is actually fairly easy to decide for most pedigrees whether one is dealing with a dominant, a recessive or a sex-linked trait, or, if the inheritance fails to conform to any of these, to postulate an irregular dominant or an irregular recessive gene. Biologists are now firmly enough convinced of the applicability of the gene theory to man, that the finding of a slightly aberrant ratio would seem to be a matter of little concern.

Such reasoning of course loses sight of the fact that the mere labeling of the mode of inheritance is of small value compared to a knowledge of the precise probabilities for predicting a hereditary condition under all possible circumstances. If the exact Mendelian proportions are not in fact realized, this might indicate a differential survival of the various genotypes. The knowledge of even small discrepancies of this sort would clearly be of great value in the consideration of eugenic problems. Or it might mean that certain genotypes are sometimes affected and sometimes normal, which is again of interest in diagnosis and eugenics. The detailed analysis of human pedigrees must therefore be encouraged, and it is hoped that the various selective processes through which such data invariably pass before they are placed on record will receive more cooperative study on the part of statisticians and medical workers.

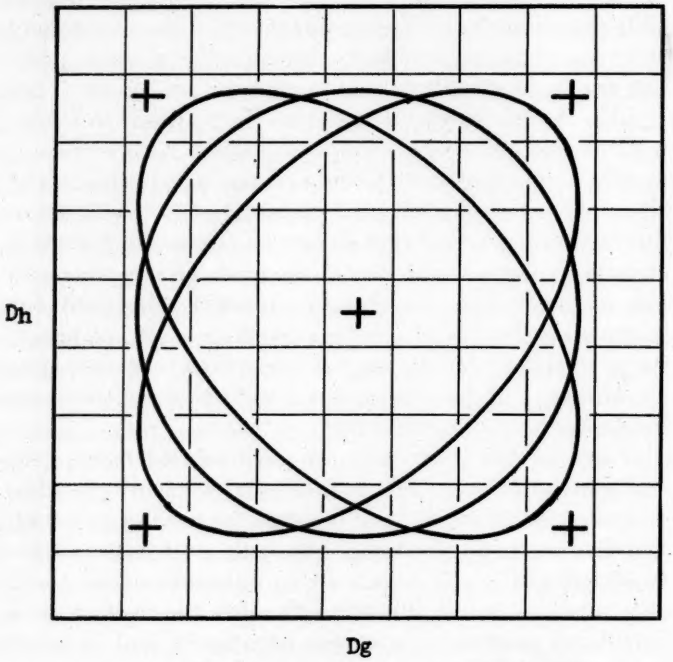
The third method to which I shall refer is the ϕ-statistic devised by Penrose (1938) for the detection of genetic linkage in man. When two genes are linked, or carried in the same chromosome, this fact is discovered in experimental situations by performing test crosses which permit all four combinations of the two characters to appear in the offspring. In the event of linkage, certain matings

will produce a proportional excess of individuals showing neither or both traits, while others will produce an excess of individuals showing the one or the other trait singly. In human data, which is usually available on only two generations, we can seldom distinguish these two sorts of mating with certainty. Also, it is frequently impossible to even pick out those matings which could definitely show one or the other effect. So we again require methods for dealing with mixed conditions which need not trouble the laboratory geneticist. In addition to fulfilling this requirement, the Penrose statistic has the advantage of being applicable to data on pairs of brothers and sisters of wholly unspecified parentage. But still more interesting is the fact that it may be applied to inherited characteristics for which even the mode of inheritance is not precisely known. It is particularly designed for metrical or graded characters showing a strong hereditary tendency but having a somewhat obscure gene mechanism. Many characters studied by anthropologists possibly fall in this class.

If two graded characters are uncorrelated in the general population, a linkage between major genes operating on these characters will not be expected to alter this fact. But if one computes deviations within sibships, or between sib-pairs, the effects to be anticipated are those shown in Fig. 3. Within some families the traits will be correlated positively, in others negatively, and in many there will be no correlation at all. The result, when many sib-pair differences are tallied in the form of a correlation table, will be a symmetrical distortion of the field in such a way as to give excess frequencies along both diagonals of the table. The ϕ-statistic, being based on the squares of the products of the differences in both traits, *D*g and *D*h, scores all the corners equally. The value of ϕ is a function of the linkage intensity or recombination fraction, χ, and its expected value rises from 0, when there is no linkage, to ½, when linkage is complete.

To illustrate the principle another way, I have set out

the expected distributions of sib-pair differences under complete linkage and under the absence of linkage for the simplest situation, wherein we assume the variations in each trait to be determined by a pair of equally common and perfectly intermediate genes. This is shown in



Penrose statistic: $\phi = \frac{1}{2}(1-2\chi)^2 = \frac{n.S[Dg^2.Dh^2]}{S[Dg^2]S[Dh^2]} - 1.$

FIG. 3

Table 2. In these tables the marginal frequencies are the same for both, so that the statements made in relation to the previous diagram can be checked here by direct comparison. In both cases, the average or over-all correlation is zero. In the case of linkage, however, the proportionality between the entries and the marginal frequencies is destroyed, with excess numbers occurring along

Dh \ Dg	-2	-1	0	1	2
2	1	12	38	12	1
1	12	144	456	144	12
0	38	456	1444	456	38
-1	12	144	456	144	12
-2	1	12	38	12	1

A. No Linkage

$r = 0.$ $\phi = 0.$

Dh \ Dg	-2	-1	0	1	2
2	4	16	24	16	4
1	16	192	352	192	16
0	24	352	1680	352	24
-1	16	192	352	192	16
-2	4	16	24	16	4

B. Complete Linkage

$r = 0.$ $\phi = 1/2.$

TABLE 2

the diagonals. In cases where the average correlation within sibships is not zero, a correction in the value of ϕ may be applied.

An application of the method to some data on human hair and eye color is shown in Table 3. The data are

Dh [Eye Color] \ Dg [Hair Color]	-2	-1	0	1	2
2	0	3	0	1	1
1	0	7	12	27	2
0	0	68	203	89	9
-1	2	21	19	13	1
-2	2	0	6	5	1

$\phi = 0.679,$ $s_0(\phi) = 0.181.$

TABLE 3. Data of Boyd and Boyd

those of Boyd and Boyd (1941) and comprise 492 sib-pairs. The value of ϕ is 3.75 times its standard error and

makes possible the assumption of a strong linkage between major genes acting on these two characters.

In cases where the precise mode of inheritance is known, there are more efficient statistics available for the analysis of linkage in human data. The Penrose method, however, is of interest because of its generality. There are probably many other genetic phenomena, which are more easily discovered under experimental conditions, but which could also be searched for in man by methods designed to detect their statistical consequences of a more general kind.

By means of these examples, I have attempted to show that certain genetic hypotheses can be tested by special methods in human data. None of these techniques requires data consisting of more than single families and some of them require even less. The absence of experimental matings and the small size of the family are seen to impinge upon such analysis to a degree less than might perhaps be expected. In any case, such difficulties are probably small compared to the present difficulties in obtaining the records in the first place. However, even here the development of such techniques may have been of some help. There are probably many more persons who are in a position to make careful studies on small groups of relatives than there are persons who can devote their study to extensive pedigrees. The realization that such fragmentary data can supply information on many genetical questions should certainly contribute to an increased interest in the study.

It is perhaps futile to make any comparison of the relative advantages of man and other species as objects for genetical study. Human genetics is unlikely to be approached from any view other than that of furthering the knowledge of man. It is tempting, however, to guess that the advantages may not be wholly on the side of the experimental species. Perhaps the chief peculiarity that has thus far been observed in human genetics is the discovery that the majority of mutant genes in man are not

recessive and that they exhibit somewhat more phenotypic variation than similar conditions studied in laboratory forms. There have been many interesting speculations as to why such conditions should prevail. In general, these explanations do not suppose that there is anything peculiar about the human gene but rather emphasize the different circumstances under which human genes must be discovered and the more variable conditions of population under which they must produce their effects. An increased interest, which Professor Dunn has called the Back to Nature movement, has recently been developed in the study of population genetics, and it is perhaps here that the study of man will be found to offer many advantages.

LITERATURE CITED

Bernstein, Felix.
1925. *Zeitsch. f. indukt. Abst. u. Vererb.*, 37: 3, 237–270.
Boyd, W. C., and L. G. Boyd
1941. *Ann. Eugen.*, 11: 1, 1–9.
Fisher, R. A.
1934. *Ann. Eugen.*, 6: 1, 13–25.
Landsteiner, K., and A. S. Wiener.
1941. *Jour. Exp. Med.*, 74: 4, 309–320.
Penrose, L. S.
1938. *Ann. Eugen.*, 8: 3, 233–237.
Snyder, L. H.
1929. "Blood Grouping in Relation to Legal and Clinical Medicine." Baltimore.

THE GENETICS OF HUMAN POPULATIONS

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THE science of human genetics concerns the material substance with which every human being starts his existence. This substance we know to be handed down to each individual through the cytoplasm and through the nucleus of the cells which contribute to his formation. As yet we do not know the total function of each of these two components of the cell, but apparently from a hereditary point of view, the nucleus with its genes is the more important part. At least the science of human genetics of to-day is concerned primarily with the distribution and the function of human genes.

A human individual may be thought of as an isolated unit which is completely independent of all other units, except for the fact that it had its origin in other units, or it may be thought of as a component of a larger unit, the population. These two units, the individual organism and the population, have many points in common. Both are integrated units made up of smaller components, and many of the functions of the components of one are similar to the functions of the components of the other. From a genetic point of view, however, the two units differ considerably. In the individual organism the components or cells all have the same genes, whereas in the population the components or individual organisms all have, or at least may have different genes. Furthermore, in the individual organism the hereditary composition does not change during the lifetime of the unit, whereas in the population it is, or at least may be, continually changing. Because of these specific genetic differences, there appear to be certain advantages in subdividing the science of human genetics into: (1) the genetics of human individuals, and (2) the genetics of human populations.

Of the two subdivisions just mentioned, the first, or the genetics of human individuals, is the more basic branch. Without progress in this area there can be little or no progress in the second. It is tempting for me to survey the basic field first but this is not my assignment. Professor Snyder has already done this in the preceding paper, and Dr. Cotterman in the paper which follows will deal further with some of its problems. I shall confine my remarks to the genetics of human populations.

The major problems of the genetics of human populations are: (1) the determination of the genetic composition of human populations at given moments in their history, (2) the discovery of the factors which change their genetic composition, and (3) the determination of the manner and the extent of the effect of each of these factors.

The determination of the genetic composition of human populations at given moments in their history is not an easy task. In fact, it is one which can not be accomplished at the present fime, because we do not know all the human characters which have a hereditary basis, and this is necessary before we can make a complete determination. It is, however, possible at the present time to determine the genetic composition of a given human population with respect to each of the inherited characters whose exact mode of inheritance is established. This can be done first by sampling the population for the phenotypic frequency of each of the characters in question, and secondly by calculating from the phenotypic frequencies the best estimates of the gene frequencies.

The sampling of the population for the phenotypic frequency of a character is accomplished by examining or testing a large number of individuals within the population and recording the percentage occurrence of each phenotype. The calculation of the best estimate of the gene frequency is accomplished by applying the appropriate formula to the phenotypic frequency. The formula to be used for the calculation of the gene frequency

is determined (1) by the mode of inheritance of the character in question and (2) by the system of mating followed within the population.

As examples of phenotypic frequency determinations which have been made and as illustrations of calculations of the best estimate of gene frequencies from phenotypic frequencies, I shall present four phenotypic frequency studies of the U. S. Caucasoid population and apply appropriate formulae to them. The four characters involved in the phenotypic frequency studies which I have chosen are: (1) the M–N blood groups, (2) taste reaction to phenylthiourea, (3) red-green color vision and (4) the A–B blood groups.

Since the selection of the appropriate formula for the calculation of the gene frequency from the phenotypic frequency is dependent in part upon the mode of inheritance of the character in question, I shall review briefly the mode of inheritance of each of the four characters under consideration. The M–N blood groups are inherited as a pair of autosomal alleles with no dominance relationship; inability to taste phenylthiourea is inherited as an autosomal recessive; red-green color blindness is inherited as a sex-linked recessive; and the A–B blood groups are inherited as a series of three alleles with no dominance between two of them, but with both of these two alleles dominant with the third.

The phenotypic frequency of each of the four selected characters in the U. S. Caucasoid population, the size of the sample studied and the name of the investigator who obtained the phenotypic frequency are given in Table I. It will be noted that some of the samples studied are rather small and, therefore, the phenotypic frequency given may not be the true phenotypic frequency of the population as a whole, but in general they may be thought of as being fairly representative.

Table II gives the appropriate formulae for the calculation of the best estimates of the gene frequencies, and also the estimates obtained by applying the formulae.

TABLE I

PHENOTYPIC FREQUENCIES IN U. S. CAUCASOID POPULATION OF FOUR DIFFERENT INHERITED HUMAN CHARACTERS

Character	Investigator	Number of individuals studied	Phenotypic frequency
M–N Blood groups	Landsteiner and Levine	532	MM 26% : MN 54% : NN 20%
Taste P.T.U.	Snyder	3,643	Taster 70% : Non-taster 30%
Red-green Color vision	Garth	795 ♂♂	Normal 92% : Color blind 8%
A–B Blood groups	Snyder	20,000	AB 4% : A 41% : B 10% : O 45%

The formulae for the calculation of the gene frequencies of the M–N blood groups, taste reaction to phenylthiourea and color vision are obviously readily derived. Those for the calculation of the gene frequency of the A–B blood groups are obtained from the square of $(p + q + r)$.

TABLE II

CALCULATIONS OF GENE FREQUENCIES FROM PHENOTYPIC FREQUENCIES ASSUMING RANDOM MATING

Character	Phenotypic frequency in U.S. population	Gene	Formula	Gene frequency
M–N Blood groups	MM 26% : MN 54% : NN 20%	A^m	$MM + \frac{MN}{2}$	53%
		A^n	$NN + \frac{MN}{2}$	47%
Taste P.T.U.	Taster 70% : Non-taster 30%	T	$1 - \sqrt{\text{homo. recess}}$	45%
		t	$\sqrt{\text{homo. recess}}$	55%
Red-green Color vision	Males normal 92% : Color blind 8%	Cb	% ♂ normal	92%
		cb	% ♂ color blind	8%
A–B Blood groups	AB 4% : A 41% : B 10% : O 45%	I^A	$1 - \sqrt{B + O}$	26%
		I^B	$1 - \sqrt{A + O}$	7%
		i	$1 - (I^A + I^B)$	67%

Many other phenotypic and gene frequency studies of the four characters mentioned above have been made. Regarding these studies in general, it may be pointed out that the populations which have been declared closely related to one another on the basis of anthropological

studies resemble one another closely with respect to most of their phenotypic and gene frequencies, whereas those populations which have been declared distantly related differ considerably with respect to most of their phenotypic and gene frequencies. A few exceptions to these rules are to be found, but this is to be expected.

In connection with this discussion of phenotypic and gene frequencies, it seems appropriate to comment briefly upon a question which has been discussed at length in the literature. I have in mind the question of how to describe a particular human population. From a genetic point of view the most satisfactory definition of a population is one which states its numerical size and describes it in terms of gene frequencies. Such definitions are specific and make possible quantitative comparisons between two populations. Of course, to be complete, a definition must include many other descriptive statements, but we need not be concerned with those here. The genetic definition of each of two populations might be presented as follows:

Population I:

N = 10,000; gene frequency = A^m 20% : A^n 80%;
T 40% : t 60%; Cb 92% : cb 8%;
I^A 60% : I^B 10% : i 30%; etc.

Population II:

N = 12,000; gene frequency = A^m 90% : A^n 10%;
T 84% : t 16%; Cb 98% : cb 2%;
I^A 30% : I^B 50% : i 20% etc.

It may not be inappropriate at this point to emphasize that two populations need not differ in their alleles to be considered genetically different. They may differ merely in the frequencies of the same alleles. Of course, they might also differ in alleles, but such differences are probably not very common between populations within the human species.

As stated above, the second major problem of the genetics of human populations is the discovery of the

factors which affect the phenotypic and gene frequencies of human populations. Apparently these factors are the same for the human species as they are for all other sexually reproducing species, namely, (1) the system of the mating followed, (2) mutation, (3) migration, (4) isolation, (5) random variation and (6) selection.

The rôle which each one of these factors plays in a given human population, or in the human species as a whole is almost unknown. Practically no systematic studies involving an analysis of changes in human gene frequencies have been made. Wright, Haldane, Fisher and others in long series of papers have worked out the theoretical consequences of the action and interaction of these factors. These analyses are of inestimable value in clarifying our thinking and in planning our program of study, but they are not substitutes for analyses of the real situation.

Although we know practically nothing about the extent to which each of the above-mentioned factors affects the phenotypic and gene frequencies of human populations, it may be appropriate to comment briefly upon each one.

The particular system of mating which is followed in a population is not important from the point of view of changing gene frequencies. Gene frequencies do not differ directly as a consequence of differences in systems of mating. However, phenotypic frequencies do. Hence, selection may operate differently on gene frequencies as a result of a difference in system of mating. For the human species as a whole there is no single system of mating which can be said to be characteristic of the species. We frequently assume random mating for human populations, but marriages in many populations are certainly far from being random. Many of them tend to be between genetically similar individuals and hence tend to lead to homozygosity. It would be extremely desirable to have a detailed analysis of the extent to which matings are assortative in the human species.

The basic change factor in any population is of course

mutation. There are not many direct reports of new gene mutations in man, but there is sufficient evidence from reliable pedigrees that many human gene mutations are occurring. Haldane (1935) estimated that the normal allele of the hemophiliac gene mutates to the hemophiliac gene about once in 50,000 individuals per generation. Compared with the mutation rate in other forms this rate is moderately high. Gunther and Penrose (1935) estimated that the normal allele of the epiloia gene mutates to the gene for epiloia at a slightly lower rate. Although these estimates are extremely interesting and enlightening, we need much more information regarding the direction and the rate of gene mutation in man before we can discuss extensively and intelligently the whole problem of human gene mutation.

Migration, which is a very common phenomenon in the human species, does not change the gene frequency of the species as a whole, but it does change the gene frequency of individual populations. Thus, for a given human population, it may have extremely important consequences. There are many reports on human migrations from one country to another or from rural districts to urban centers, but from a genetic point of view most of these reports are of little value. They tell us very little about the distribution of genes, primarily because we know very little about the genetic composition of the individual migrants or of the populations involved.

Isolation undoubtedly played a very important role in the early differentiation of man into primary stocks and races. To-day there still exist certain voluntarily isolated populations and some involuntarily isolated groups, but in general there is a tendency toward the disappearance of isolating barriers. It seems that some day there will be complete admixture of all peoples.

Random variation is a factor which is seldom appreciated as an important factor in changing gene frequencies, but apparently it may be extremely important in small populations. By random variation is meant the variations which occur as a result of chance and bear no

relation to the survival value of the gene. It seems probable that some of the striking differences between the gene frequencies of American Indian tribes and between other small populations which have been found are due almost exclusively to this factor.

Of all the factors which affect phenotypic and gene frequencies, natural selection is probably the best known. Some have questioned its operation in the human species, but regarding that point there is no question. Members of the human species which are not adjusted to their environment die or fail to reproduce as do members of lower species. We may, however, question whether the environment man has created is the one which permits the most desirable members to survive, but that is another problem. That question I shall not discuss.

Thus far we have reviewed some of the facts and some of the problems of the science of human population genetics. A fair question to ask now is, of what value is a study of the genetics of human populations? This is not an easy question to answer, but probably the first one which comes to mind at the present time is the simple answer that it acquaints us with the genetic composition of our nation's population and hence, to a large extent, with the health of our nation's man power. I should not claim that the genetic information which we have available at the present time would be of much value in the present emergency, but if we had systematically studied the last few years, many small populations with respect to all the characters we know to have a hereditary basis, we should now have an invaluable fund of information.

Another value of the study of the genetics of human populations is that it throws light on the interrelationships of different populations. So far, the separate studies may not have clarified any particular relationship, but it seems certain that they will, as more characters are studied. An interesting result of human gene frequency studies is that they not only make us aware of differences between human populations, but of similarities as well. Apparently all members of the human

species have identical gene loci. Furthermore, most populations apparently have nearly the same alleles. These alleles may differ in frequency, it is true, but the same genes are present in the population. Thus, basically, the populations are not different. This emphasis upon similarity, I think, is just as important and justifiable as the emphasis upon dissimilarity.

A third value of a study of the genetics of human populations is that it gives man an appreciation of the manner and of the direction in which he is evolving. Some may read into this statement an argument for a eugenic program. It is not intended to be that at all. In fact, I should like to see the science of human genetics developed completely apart from any desire to improve the human species. I believe that by keeping human genetics a distinct science we will not only serve our science best, but society as well. Of course, if some of the information which is gained by human geneticists can be of value to others who are interested in improving the human species, that information should immediately be made available to them.

Regarding a eugenic program, I might say this: There is little evidence from an analysis of the genetics of human populations that we can change appreciably man's hereditary make-up, at least, not in the course of a few years. However, at the present time, no one can be blamed for wishing that he might be able to do so, and no one can be blamed for wanting to do so.

LITERATURE CITED

Garth, T. R.
1933. *Science*, 77: 333–334.
Gunther, M. and L. S. Penrose
1935. *Jour. of Genetics*, 31: 413–430.
Haldane, J. B. S.
1935. *Jour. of Genetics*, 31: 317–326.
Landsteiner, K. and P. Levine
1929. *Jour. of Immunology*, 16: 123–131.
Snyder, L. H.
1929. "Blood Grouping in Relation to Clinical and Legal Medicine." Baltimore: The Williams and Wilkins Co. 152 pp.
1932. *Ohio Jour. of Science*, 32: 436–440.

FUTURE POSSIBILITIES IN HUMAN GENETICS

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IN consquence of the extremely unsettled conditions to which civilized human society is, at the present time, subjected, scientific research is biased in a direction which favors lines of inquiry which promise to give effective results within a short space of time. Consequently, the present tendencies of research in human biology lean towards physiology and practical psychology rather than towards genetics. People desire to know the immediate capacities of different men and women and are not much interested in discovering how to ensure that members of future generations will have specified genetic constitutions. The knowledge of the genetical composition of a given individual sets the limits within which he may be expected to react in various known environments; it can not, however, enable accurate predictions to be made about what will happen in quite different environmental circumstances. Moreover, even when attention is concentrated on inherited characteristics, which are inappreciably influenced by environmental changes, the type of inference, which a thorough understanding of genetical structure makes possible, will usually be expressed in a rather modest degree of probability. Though predictions about the genetic status of an unborn individual can rarely be exact, predictions about the prevalence of inherited characters in sibships or in large samples of the population are capable of being very precise. Nevertheless, there is no escape from the conclusion that the study of human genetics is, in the main, a long-term investment of time and energy, from which returns must be expected at first to be small.

Human genetics is a broad subject and its borders are somewhat nebulous, but it has, at least, four fairly distinct

fields of study. They are not really separate from one another but, for convenience, they may be described as the biological, the clinical, the mathematical and the social. The first field, which develops out of embryology and animal genetics, begins, for example, with the physiology of reproduction, the biology of such processes as twinning and the histological investigations, in man, on the behavior of germ cells with special reference to chromosomes. Since man is an experimental animal only to a very limited degree, the inferences drawn in this field are often indirect. Up to the present time the direct observations made on human cells have demonstrated the presence of 24 pairs of chromosomes, but it will be some time before each of these can be individually recognized. No gigantic specimens of chromosomes have yet been brought to light and there are still differences of opinion as to whether the Y-chromosome is always present in the male. When more information is available about the details of morphology and behavior of the human chromosomes, a tremendous impetus will be given to the other branches of the subject.

The second field is mainly a clinical study. It is concerned with the precise identification, in subjects presented for genetical examination, of characters due to single genes. Unless the definition of genetic characters is technically exact, there is no means of knowing whether two families recorded by different investigators, or even by the same investigator, can be treated as examples of segregation of the same genetic effect. Fortunately, serological blood tests and chemical tests of urine can be used with precision for the identification of quite a large number of genetic peculiarities. In the early days of human genetics, investigators were almost confined to the search for simple Mendelian characters. This field, indeed, is still proving a fruitful one and has been enriched both by the theory of gene frequencies in random populations, the understanding of the effects of inbreeding and the numerical analysis of ratios in sibships. All this

work presupposes that the characters studied segregate clearly and that their presence or absence in a given subject can be ascertained with certainty. The techniques developed for identification of some of these hereditary characters may become aids of much practical value in medical work unconnected with genetics. Thus, the fact that color blindness and night blindness can be detected, taken together with the knowledge that they are inborn peculiarities, may be of service in the study of aptitudes. Similarly, the recognition by Landsteiner and his coworkers, of iso-agglutinins and other idiosyncrasies in the blood has made a highly significant contribution to medicine and surgery. In general, it is desirable in clinical medicine to know when we are and when we are not dealing with an inborn peculiarity—irrespective of our ability or inability to predict its occurrence. The direct attack upon some of the commoner ailments, however, to determine how far they represent inherited dispositions, has not always been as successful as might have been hoped. The identification of a condition is sometimes comparatively easy, as in diabetes, epilepsy or vascular disease, but the mode of inheritance is found to be extremely complex. Usually it can be surmised, not only that many genes play a part in the causation, but also that environment—prenatal, intranatal or postnatal—alters the appearances of the signs and symptoms. The attempt to keep the hereditary part of the causation constant by investigating twins has not proved to be an instrument of such decisive value in genetical study as Galton originally supposed it would be. The environments of monovular twins are usually not sufficiently diverse for much information to be obtained from this source about environmental modification. Moreover, the differences found between monovular twins are not always environmental in origin; there may be, according to Dahlberg, genes whose effects are asymetrical; also somatic mutation can occur in one member of a pair and not in the other. The study of the genetics of twinning itself is, in fact, becoming a much more interesting subject than the study of

twins from the point of view of concordance and discordance of characters supposed to be due to heredity. The investigation of twins has also helped to stimulate the formulation of many techniques for the exact recording of human biological data. Unfortunately, some of the characters which can be most accurately measured are extremely complex genetically. For example, dermatoglyphs, which appear superficially to fall into discrete types, on quantification by ridge counting or other methods, reveal graded tendencies like measurements of height, weight and mental capacity. Occasionally, as shown by Hurst and Davenport in eye color and by Wiener in allergic tendency, graded distributions are trimodal. In such circumstances, intermediate genes of major significance can be postulated. Taste deficiency for phenylthiourea, on the other hand, seems to have a graded bimodal distribution and the dominant and recessive genotypes can be specified. The genetic analysis of graded human characters, when environmental variations have been eliminated, presents a major problem for the future.

The third part of the study of human genetics is the arithmetic of probabilities of occurrence of known characters in different sibships. This, in the initial stages, is a calculation by use of Mendelian principles of the chances that children will be affected in one way or another, when the mode of selection of the family is specified. Not all human hereditary characters follow Mendelian rules, however, and in the arithmetical analysis of sibships which contain malformations, possibly due to chromosome abnormalities, there are many traps for the unwary. The next stage is to ascertain relations, of a topographical nature, between different genes so that predictions about concurrence or divergence of traits in given families can be made. In this field, theoretical work has outstripped the collection of factual data. The detection of linkages in man, already advanced as far as the sex chromosome pair is concerned, promises to become a branch of science, which, like astronomy, is esthetically

stimulating but must not be expected to have practical uses obvious to the layman.

The fourth branch of human genetics includes the study of the social biological problems of race, population and fertility. These subjects are mainly advanced by inquiries which cover large populations. The ascertainment of gene frequencies, of fertility rates and of the incidence and causation of abortions are relevant here. Many people, especially the politically minded, wish to use facts already ascertained in this field for furthering their ideals of what future generations should be like. There are some types of population surveys, like the recent one by Bell on consanguinity, which give valuable help to clinical genetics. The natural order, however, is for social biological work to follow after the first three fields of genetical study have become well established. The desire to make social improvements in the human race, however, by scientific control of breeding has been so strong that many premature inferences have been drawn and many policies advanced upon insufficient evidence. Eugenics is hampered by lack of knowledge of relevant facts, and the "improvement" of race is likely to be a hard task even when knowledge of heredity is adequate to sanction deliberate large-scale selective breeding in man. We need to have a lot more information about the effects of natural and social selection in man in past ages and about the mutation rates of genes. This information will eventually be obtained from extensive investigations of human populations. Special attention will have to be given to differences in familial appearances and modifications of the same genetic characters in different genetic and environmental settings. According to Haldane's estimate it will take the human race about as long to learn how to control its own nature as it has taken already for it to learn how to control its environment. If this is true, it is indeed well that it should be so, for the results of man's ability to control his environment have, so far, been far from satisfactory in terms of human happiness. It is perhaps fortunate that the branch of the subject which is growing

most rapidly is the second one. Clinical genetics, as part of medical science, is of neutral value from the ethical point of view and primarily concerned with individual health.

Though the results of human genetics so far obtained may be of relatively minor significance in the future of the human race, the future of human genetics itself depends very much upon the future trends of society. How far, for example, is world opinion ever going to allow experimental human breeding? It is fortunate that the human population is so large, that there are in existence at any time almost enough kinds of matings to satisfy any experimental requirement. The problem is to locate and examine the material, which already exists, rather than to create new material. Apart from the question as to the comparative values of long- and short- term investigations, the general attitude of people towards the desirability of genetical study is important and is of more significance here than in some other branches of science. Religious dogmata interfered with the growth of medicine in the Middle Ages and modern political ideas may interfere with the growth of genetics. If individuals object to being examined or to having to give histories, there is a loss of potentially valuable information, but if governments decide that genetical facts must be collected or interpreted in special ways, this may seriously handicap the advance of knowledge. In order to make rapid headway in this complex field, the organization of groups of scientific workers with special skills in clinical, chemical, immunological and metrical techniques is essential. It seems, moreover, impossible to get such groups together without the assistance of public bodies and the goodwill of the state. Only when the time comes for such units to be organized more widely than they are at present, and when large numbers of skilled persons are employed in obtaining genetical facts (instead of leaving these to be collected by interested people as a leisure time pursuit), will substantial and rapid advances in the knowledge of human heredity be made.

TWO DECADES OF EVOLUTION THEORY[1]

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To use most effectively the time allotted to me for review, which averages 45 seconds per year, I shall assume that evolution theory has developed in accordance with the principles which govern the growth of other organic things, and that the curve of emphasis should be of exponential type. Furthermore, human interest in any past event diminishes rapidly as that occurrence recedes to yesterday and yesteryear, more slowly as it retreats through the decades, but makes little distinction between the happenings of distant centuries. Accordingly, I shall pass over the opening years of the period under scrutiny with only a brief outline of their accomplishments, and linger only moderately over the central span, in order to dwell at some length upon the last bi- or triennium.

The early nineteen twenties witnessed no important frank and unconcealed forward movement in evolution theory. Knowledge of the architecture of the germ plasm was being elaborated in important ways during that time. Every one deeply interested in evolution principles recognized that in some fundamental way they were bound up with genetic principles, but establishing their precise relationship was not a task to be lightly undertaken. This difficulty in putting evolution upon a genetic basis was a most fortunate circumstance, since it allowed time for the genetic processes to become better understood. Any attempt to provide a genetic explanation of evolution at an earlier time than it actually was done must have been only partly successful, if not an outright failure; and to have corrected later the faults of such premature speculation would have been more costly of effort than to build from the ground when the time was ripe. However, at

[1] Part of a symposium on Two Decades of Zoological Progress presented before the Michigan Academy of Science, Arts and Letters, March 14, 1941. Contribution from the Department of Zoology, University of Michigan.

least one geneticist goes farther than this, and proclaims that even the delayed genetic explanation was devised too soon. It must be done all over, and he proceeds to do it all over. But of that, more later.

The genetic explanation which was fortunately not attempted earlier, or which was offered too soon, according to one's point of view, was a mathematical analysis of gene populations, in obedience to some general rules of behavior, and under the influence of various biological conditions. Computations designed to be of wide application must be based on generalized processes and recurrent situations. The more inclusive of these studies postulated mutation of genes, usually recurrent mutation, and the random assortment which independent chromosomes provide, with stipulated degrees (including completeness or lack) of dominance. Particular genetic situations were treated in more specialized works. The phenomena named are common enough to warrant a mathematical consideration. They are the subject matter of what Goldschmidt,[2] in a tone of mild disparagement, calls "classical genetics." Bearing upon these genetic phenomena, in the mathematical studies, were such external influences as selection (as measured by number of descendants), migration (as affecting certain areas), pure accident (affecting not only the external but also the genetic factors) and size of population as influencing the speed with which the genetic factors would work. The leading names in this statistical movement are those of Wright, Haldane and Fisher, but there are others. As relating to random gene distribution in geographic races, perhaps involving migration, Dobzhansky has been a leading worker, but the honors have been shared.

No one supposed that these calculations told the whole story of evolution. The authors of the pertinent works made no claim to exclusiveness of their application; in-

[2] R. B. Goldschmidt, "Material Basis of Evolution." Yale University Press, 1940.

deed, they understood better than any one else that some features of evolution belonged to fields wholly outside the mathematical one they had cultivated. Some biological factors of evolution were so much more important in a qualitative sense than in a quantitative one that a statistical study of them would be of minor significance. The mathematical discussions were frankly and avowedly a fractional contribution to evolution theory; they were never designed to supplant all earlier proposals, nor to make later ones unnecessary.

How great a portion of the evolution process might be attributed to the workings of the "classical" Mendelian scheme under the influence of selection, chance, migration and mutation, probably no two biologists have precisely agreed. A decision on this point would require a weighting of mere change as contrasted with the separation of species, and there is no agreement concerning their relative importance. But perhaps we do not need to agree, for of late the value of the statistical studies has been questioned. That the Mendelian system would not work as stated, under the conditions stipulated, is not claimed; but that the results have anything to do with the major features of evolution is denied. The doubt and the denial have been planted and have flowered most conspicuously in Goldschmidt's evolutionary gardens, but in part it is a community project. Whether or how abundantly they will fruit only time and its ripening effects on judgment will tell. Let us see what it is that is criticized.

Mutation itself was the first to receive a major blow when the suggestion was made that the differences which arise under that name were not alterations of single genes, but rearrangements of chromosome parts. At times it seems as if genes are abandoned, though just what could be accomplished by rearrangement of chromosome material if this material were homogeneous, and just how a differentiation among the parts of a chromosome would differ from genes, is not clear. It is conceivable that many of the changes called mutations have been

mere rearrangements of genes, without gain or loss, and without change except that of position; and position effects are well known. But it is not a little surprising, if only rearrangement is involved, that a given part of a chromosome transported to a new place in the system often does so nearly the same thing as in its "original" place. It is also conceivable that changes of position sometimes carry with them minute gains or losses which are not detectable as such, and that some position effects partake also of the nature of real mutation. A definition of mutation would be required to decide such points. However, it is not the reality of mutations, and not their nature, that is most at issue in the new doctrine; it is their significance that is challenged.

The role of mutation, in the new theory, is confined within the species. It diversifies breeding populations; it even leads to geographic races, many, perhaps most, of which are adaptive. Races of the gipsy moth, and of some of the mammals, are found to be adaptive, and it is easy to carry over the idea of adaptation to the many other races which give no reason for suspecting their fitness to environment. Adaptiveness of races is not, however, an important feature of the great scheme of evolution, it is held. Races, and individual variations not in any way geographically separated, are of concern only to the one species within which they occur. They are of no advantage to the species except as they lead to adaptation, and are of no significance beyond that species. Their production Goldschmidt calls microevolution. "Classical genetics" is capable of explaining them, and the statistical studies may be expected to show something of the order underlying the process.

The thing which microevolution is unable to explain, according to Goldschmidt, is the origin of species. Mere accumulation of small genetic differences is not enough to make them different species. Here he takes issue with innumerable evolutionists both present and past. In this contention, we should agree with Goldschmidt, but the

argument leading to that conclusion may sometimes be fallacious. Were mere accumulation of differences all that is necessary to separate species, producing between them a bridgeless gap, old species should show the gap more markedly than young ones. Goldschmidt implies that this argument goes in circles when he describes it as follows: "Why the bridgeless gap? Because the species are old ones. Why are they old ones? Because of the bridgeless gap between them." The fallacy of this criticism lies in the two meanings of "why." The first "why" asks, What is the cause? The second asks, What makes you think so? There is no circle in this argument. But it is not necessary to charge circular reasoning to reject the thesis that mere number of differences between types creates the gap which separates them. There must be something deeper.

What, then, does separate species? Goldschmidt holds that the attainment of a different "reaction system" is the criterion of the origin of a species. What does this expression mean? It is important that we have a definition. A definition that can be concretely applied is preferable, but one that is applicable in principle is mandatory. We could if we wished argue in a circle, and say that a new system had been produced when a new species arises; and if asked when that had happened, reply that it happens when a new system is produced. This sort of reasoning will be necessary unless some criterion of difference between reaction systems can be devised. Contrasting these systems with groups of atomistic genes does not help; it merely raises the question of the relation of parts to wholes. I would like sometime, somewhere, to express some views on that question, but this is neither the time nor the place.

Change of reaction system is assumed to be occasioned sometimes, perhaps regularly, by such chromosome rearrangements as inversions and translocations. By these rearrangements there are set up, Goldschmidt holds, two chromosomal systems which are incompatible with one

another. Were such rearrangements certain to produce incompatibility, distinctions between species could be discovered by cytological observation in one order of insects (Diptera) by study of one organ (salivary gland). Mere rearrangement is not enough, however, since inversions and translocations may take place within the species. That is, some such repatterning does not amount to erecting a new system. Yet in some way whole chromosomes or groups of chromosomes are held to govern compatibility with other chromosome systems. In what way do they do so? The answer to this question is what is needed to arrive at the definition just demanded.

In seeking that answer, perhaps we may use the other half of a principle of which Goldschmidt uses one half. As he points out in discussing F_2 hybrids of two species, "a simple Mendelian behavior is only visible when expected." If we see only what we look for, we should look for many things. We need not be too concerned lest "classical genetics" of the text-books be found wanting in this particular emergency. It is a long time since any geneticist put his whole conception of genetic processes into a text-book, or presented it before his elementary classes. Let us look for something less simple, but something which can at least be defined.

Just what is the criterion of a "new reaction system?" Some chromosomal rearrangements produce one, others do not, hence they can not be used. The unbridged gap between characteristics is helpful in indicating where to look for different reaction systems, and is a common tool of systematists. Yet this gap, while it usually marks a difference of reaction system, is at fault because it overlooks some such differences; witness the two species of Drosophila whose differences were not observed until after their reaction systems were otherwise proved to be different.

In the absence of an easy visual criterion of difference in reaction systems, how shall one proceed in the practical labors of systematics? A new system has been created

when it will not work along with the old one. The way in which this ability of two systems to work together can be tested is to mate two individuals possessing the two systems, to see whether, or how freely, they will reproduce. If they reproduce freely, and normally reproducing offspring result, the systems are compatible; they are the same system. If they do not reproduce, or do so only haltingly, or if their offspring have reproductive disabilities, the two systems are different. If one of them arose from the other, a new system has been created. Whatever reaction systems may be, it is difficult to imagine any other criterion of distinctions between them than the test just named.

Now we are on familiar ground. One recognizes an old acquaintance, despite the new name under which he travels. Such distinctions between reaction systems have long been made by evolutionists, who considered that they were testing interfertility and intersterility. The name isolation is often used, but apart from occasional geographic or temporal separations it means the same thing. These evolutionists would usually agree with Goldschmidt as to the distinction between species; they have differed chiefly in regarding the attainment of specific difference as marked by the advent of intersterility, rather than by the production of a new reaction system. This statement intentionally overlooks the fact that some species, as recognized by taxonomic workers, are not intersterile, even fractionally. Such species mean nothing in the present discussion, for they must also have the same reaction system.

The search for intersterility has the advantage of being definable. One can discover when it has arisen, and can turn attention to its causes. Perhaps these are frequently chromosome rearrangements. But may they be something else? Let us pass by the accumulation of small changes which would make one phenotype very different from another. Unless there are among them some changes that affect reproduction, the two phenotypes should still be interfertile; they should possess the same

reaction system. If some of the changes do affect reproduction adversely either immediately or in hybrids or their descendants, a degree of intersterility has arisen; the reaction system set up by the change is a new one. And if only certain changes affect reproduction, it should not always be necessary to await the accumulation of many differences; the reproductive changes may occur early. Intersterility—a new reaction system—may arise before there are many phenotypic differences; again, witness the two species of Drosophila whose intersterility was the first-known sign of specific distinctness.

Goldschmidt points out that considerable phenotypic differences between two species could be due to a single genetic change, be it gene mutation or chromosome rearrangement, working through a hormone with many developmental responsibilities. Differences appropriate even to higher taxonomic distinctions (families, orders) are sometimes due to a simple genetic change, though one would hesitate to accept Austin H. Clark's[3] view that divisions of phyla originated early by single steps. No such large changes accomplish the initiation of species, except as the bent of mind of taxonomists may attribute that result to them, unless they involve or are accompanied by intersterility—the production of a new reaction system.

To what extent chromosome rearrangements produce both intersterility and phenotypic differences is not known. There are doubtless some which do both, some which produce phenotypic modification without affecting reproduction in the hybrids, and perhaps some which entail intersterility without important visible effects. The possibility remains, also, that gene mutations may do all these things. If they do, they produce a new reaction system, by any standard that can be applied. The great genetic problem of evolution is still to discover the cause or causes of intersterility. Any new name which will stimulate the search for these causes will be welcomed by the genetics-evolution fraternity.

[3] A. H. Clark, "The New Evolution; Zoogenesis." 1930.

DIVERSITY OF ENDOCRINE FUNCTION IN THE REPRODUCTION OF VIVIPAROUS FISHES

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INTRODUCTION

VIVIPARITY has arisen repeatedly in teleost fishes. In some orders most of the families are viviparous, but this type of reproduction has apparently originated separately in each family. Some instances occur in single genera or species of families, the other members of which are oviparous. Various degrees of modification of the usual sequence and length of time involved in ovulation, fertilization, gestation and hatching have evolved in the different types of viviparity.

In viviparous mammals the development of the gonads and of the secondary sex characters, as well as the processes of ovulation, implantation, cyclical changes in the uterus, quiescence of the uterus during gestation and activation of the uterine muscle during parturition, are partially under endocrine control. It is becoming evident that these same features of development and reproduction in viviparous fishes are controlled in part by the same agents. In fact, a number of mammalian hormones, such as testosterone propionate, ethinyl testosterone and pituitary hormones, have been used successfully in fishes in changing the usual course of ovulation, retention of embryos by viviparous fishes, the development of the secondary sex characters and the time of development and character of the gonads. It is the purpose of this paper to review the events of reproduction in the various types of viviparity in fishes and in the light of our present information on the hormone control of reproduction in teleost fishes to indicate some of the facts in the parallel adaptations in the endocrine control.

There is much variation in the length of the gestation

period. In some fishes where viviparity is incipient, fertilization is internal and the embryos are born in a very immature state. In some of these species there is a very elaborate copulatory mechanism in the male, but, as far as the female is concerned, there are practically no adaptations for viviparity. At the opposite extreme are some members of the family Embiotocidae (*Amphigonopterus,* Hubbs, 1921) in which the embryos are retained until the males at least are sexually mature. There are many intermediate stages in which the embryos are retained for periods of varying lengths of time.

In some instances the degree of dependence of the young embryos upon the parent female is very slight. The case of *Gulaphallus mirabilis* (phallostethid fish) is one in which there is practically no dependence of the embryo upon the parent (Villadolid and Manocop, 1934). In poeciliid fishes which have a fairly simple type of viviparity, the fact that embryos may be removed from the ovary of the parent female as much as fifteen days before birth and can be maintained alive in aerated fish Ringer's solution, indicates that there is an ample yolk supply for the entire gestation period and that the embryo depends upon the parent only for respiration and the evacuation of wastes. A number of highly specialized viviparous fishes have an exceedingly small yolk supply and at the same time the gestation period is prolonged. In such cases the embryos must depend upon the parent for a food supply as well as for respiration and waste evacuation (Turner, 1940a, 1940b, 1940c, 1940d). Numerous intermediate stages between those which depend least and those which depend most upon the parent occur even in species within a single genus.

While all embryos are retained within the ovary in viviparous teleost fishes so that the ovary functions both as an ovigerous organ and as a "uterus," there are two different positions in the ovary which are occupied by the embryos. In all cases in which viviparity is pronounced, fertilization takes place in the ovarian follicle. In one

type of viviparity the embryos are retained within the ovarian follicles, which in some cases become highly modified during gestation. In the other type the embryos are evacuated in early stages into the ovarian cavity, where they pass a long period of gestation. Highly specialized viviparity is found in both types.

Associated with the difference in location of the embryos in the ovary are differences in degree of modification of the ovarian tissue itself. These differences are associated also with the length of the gestation period and with the abundance of yolk in the ovum. In those cases in which there is a retention of the embryo in the ovarian cavity there is an earlier fleeting embryonic development in the ovarian follicle. Where the embryos are retained for a long period within the ovarian cavity there are extensive cyclical changes in the epithelium, the vascular supply and the stroma of the ovary. Where embryos are retained in the ovarian follicles and have an abundance of yolk, there is little change in the follicles other than its encapsulation and an increase in the vascularity. If the yolk is very scanty and the embryos are retained in the follicles for a long period, a pseudo-placenta is developed between the expanded pericardial sac or coelomic sac of the embryo and the internal follicular walls which become well supplied with villi (Turner, 1940a, 1940b).

Viviparity is found in some fishes in which there is a seasonal periodicity and an annual reproductive cycle (*Embiotocidae*). During the reproductive season there is a shoreward migration and in the shallow water evacuation of young and copulation take place. There is a close resemblance between the reproductive behavior of fishes of this type and that of many marine and fresh-water oviparous fishes which have an annual reproductive cycle. Other viviparous fishes, particularly those which inhabit the tropics, have short cycles in which young are reproduced every two or three months. A still shorter cycle of about one month exists in typical poeciliid fishes. Usually in poeciliid fishes one brood is evacuated before a new

group of ova is fertilized by sperm stored in the ovary or acquired by new copulation. In some specialized poeciliids, however, one or more new groups of ova may be fertilized during the gestation period of an older group of embryos and in extreme instances as many as nine small broods may exist in an ovary at the same time (Turner, 1937, 1940a). Groups of öocytes will be maturing at the same time and gestation is practically continuous. This phenomenon of effective superfetation is possible only in that type of viviparity in which the embryos are isolated in ovarian capsules. The ovarian cavity does not seem to be a favorable site for the development of more than one brood at a time.

Summary of diversity in viviparity: (1) Periods of gestation in different species of viviparous fishes may be short, intermediate or long. There are different degrees of dependence of the embryos upon the maternal parent for respiratory products, the evacuation of wastes and a food supply, from practically complete dependence to almost none. (2) Embryos develop in two different sites within the ovary, either encapsulated ovarian follicles or the ovarian cavity. The extent to which ovarian tissue is modified varies particularly with the length of the period of gestation, the type of viviparity and the amount of yolk in the ova. (3) Viviparity occurs in species which have an annual period of reproduction, in other species in which the reproductive periods are of one month or more duration, and in highly specialized cases in which a number of broods exist in the ovary at the same time.

OVIPAROUS FISHES

Ova which are to develop into embryos in a single season may come to maturity all at the same time in typical oviparous fishes, and in spawning all are evacuated at the same time. In other instances ova come to maturity over an extended period of time so that ovulation and spawning occur over a period of several months. In all, fertilization is external. The embryos

develop within the chorion for a length of time which is dependent upon the amount of yolk in the egg. Hatching occurs with the rupture of the chorionic membrane and the freeing of the embryo as a larva. The sequence of events in typical oviparous fishes is as follows: ovulation, involving rupture of the ovarian follicle; evacuation, involving activation of the musculature of the ovarian wall; external fertilization; external development of embryos within the chorion; hatching; further development to maturity.

The important events in reproduction in oviparous fishes are apparently controlled by pituitary hormones. The stimulation of the ovarian follicle to elaborate mature öocytes may be augmented by the addition of pituitary substance injected into the coelomic cavity with the result that eggs are formed long in advance of the regular season. There has been considerable work which demonstrates that ovulation may be caused prematurely by a similar treatment, indicating that the process is caused by a pituitary hormone which, when it reaches a seasonal threshold point, causes the follicles to rupture and expel the eggs into the ovarian cavity. The strong contractions of the ovarian muscles which are responsible for evacuating the eggs from the body during spawning do not occur at other seasons and it may be presumed that this function, as in mammals in the evacuation of embryos, is also under pituitary control.

Incipient Types of Viviparity

In the phallostethid fish *Gulaphallus mirabilis* (Villedolid and Manocop, 1934), the male has an elaborate structure for the intromission of sperm, but after the eggs have been fertilized in the posterior part of the ovarian cavity the embryos are evacuated from the body in very early stages. Here there is a slight shift in the sequence of the events of reproduction, fertilization preceding evacuation of the embryos. Otherwise the situation is identical with that in oviparous fishes. No change

in endocrine control would be necessitated. Viviparity in *Sebastodes caurinus,* in *Sebastes marinus* (Williamson, 1911) and presumably in other scorpaenid fishes is slightly more complex. Reproduction is seasonal and annual. The sequence of events in these fishes is as follows: fertilization; ovulation; a short development of the embryos within the ovarian cavity; evacuation of the embryos in a fairly early stage (birth); hatching and final development. The fact that there is a retention of a large number of embryos in the ovarian cavity may indicate that a lack of a pituitary hormone at a threshold level is responsible for quiescence of the ovarian musculature during the time in which the embryos are retained.

SIMPLE VIVIPARITY IN POECILIID FISHES

In this type of viviparity the ova contain enough yolk to furnish embryos with nutritive materials for the entire period of gestation, which lasts more than twenty days. The ova are fertilized in the follicles which later become vascular capsules, but which are otherwise unmodified. At the close of gestation the embryo is freed from the capsule into the ovarian cavity and in the process, the wall of the capsule and the chorion which has surrounded the embryo up to this time are ruptured. Ovulation and hatching therefore take place almost simultaneously. Contraction of the muscular walls of the ovary expel the embryos through the gonaduct and vent to the outside almost immediately. The processes of birth and hatching have been studied in detail by the writer in *Gambusia affinis* by observing the process of birth in living specimens and by killing and fixing females during the process of birth. As many as four embryos may be expelled from the ovarian cavity by a single muscular contraction, but they pass through the vent singly; a single wave lasts about four seconds and expels all embryos which have been evacuated into the ovarian cavity from the follicles since the last wave. The waves of contraction occur at intervals of from thirty seconds to three minutes. All

embryos that have come to maturity in a single brood are evacuated from the ovary within the space of about forty-five minutes. The writer is convinced that the rupture of the follicular capsule and the liberation of the embryos into the ovarian cavity is identical with the process of ovulation in oviparous fishes. The following observations are offered in support of this point of view. The process, when observed in the living state, closely resembles the process of ovulation seen in frogs and oviparous fishes. All embryos are expelled at about the same time. The agents which might be responsible for the rupture of the follicle could be the movement of the embryos themselves or the violent muscular contractions of the ovarian walls which would rupture the follicles or a pituitary hormone causing ovulation. In cases where there is superfetation and more than one brood of embryos occurs in the ovary at one time, rupture of ovarian capsules occurs only in those follicles containing the older embryos. The process may be viewed in the living specimens by pithing the female, opening the body cavity and slitting the ovary so that the internal surface is exposed. Small oval apertures arise at the point of rupture and gradually extend. The embryos are evacuated from the follicles by the elastic tissues of the capsule wall itself. There is seldom any movement on the part of the embryos.

The order of the processes concerned in reproduction is changed in this type of viviparity. Fertilization occurs within the follicle and it is followed by embryonic development for a period of more than twenty days without ovulation. Ovulation and rupture of the chorion (hatching) occurs simultaneously and birth follows within a few minutes. It is not known whether the heavy muscular contractions which expel the embryos from the ovaries occur at other times, but there is a suggestion that they are synchronized with ovulation and are under hormone control.

As far as the relationship of ovulation and birth are

concerned in comparison with reproduction in oviparous fishes, nothing new in endocrine control is suggested since, in both, ovulation is followed by a contraction of the ovarian muscles sufficient to expel either ova or embryos through the vent. However, ovulation is postponed for a long period after maturation and fertilization of the ovum, indicating that the attainment of a threshold level of the pituitary hormone responsible for ovulation is long delayed. Injection of pituitary substance into the body cavities of gravid females of *Cnesterodon* (Houssay, 1930), will cause early ovulation and the birth of immature embryos.

There is a difference in reproductive periodicity, also, between the seasonal oviparous fish and the simple viviparous poeciliid. The stimulation of the ovary to form mature ova is under pituitary control, although environmental factors such as temperature, food and light play a role. The short and repeated cycle of the poeciliids as compared to the longer annual cycle can occur only in the presence of a modified hormone control.

A similar type of viviparity occurs in the hemirhamphid fish, *Dermogenys pusillus* (Smith, 1926), but the interval between reproductive cycles is longer. The same type of hormone control is suggested.

In the anablepid fishes (Turner, 1940b) a type of viviparity exists which in some respects resembles that of the poeciliid fishes. However, the yolk of the ova is extremely small in amount, the mature ovum being less than 1 mm in diameter. The embryos are retained for a long period and reach a length of 47 to 55 mm at birth. There is a highly developed pseudo-placenta in these forms. The sequence of the events of reproduction is the same as in the simple poeciliid fishes, but the type of viviparity differs in that there is a longer retention of embryos and a greater dependence of embryos upon the maternal parent during gestation. It is possible that the stimulation necessary for the formation of the pseudo-placenta might be provided by a hormone.

Poeciliid Fishes with Superfetation

Some species of the genera *Poecilistes* and *Poeciliopsis* have simple superfetation (Turner, 1937). A second group of ova are fertilized after a first group is well advanced in gestation. In this type of viviparity there are no embryonic adaptations beyond those in poeciliid fishes with single broods. In some other species of these genera and in *Aulophallus* and *Heterandria,* there are multiple broods; as many as nine broods of small embryos may occur in an ovary at the same time. In all the latter there is a poor supply of yolk in the mature ova and the embryos draw most of their food supply from the maternal parent by means of a pseudo-placenta and presumably evacuate wastes by the same means.

Hormone control, causing production of mature ova and also ovulation, must differ from that of the seasonal oviparous fish and to a greater degree than in poeciliid fishes which have one brood at a time. If the short cycles are assumed to be the often-repeated equivalents of the annual cycle of oviparous fishes it would be necessary to assume also that the hormones controlling follicular stimulation and ovulation would be maintained at an almost constant high level or that they would be increasing and receding so as to reach a threshold point at very frequent intervals. If, on the other hand, it be assumed that a single annual cycle exists with the production of the individual broods representing subdivisions of that cycle, it would be necessary still to assume that the controlling hormone is being maintained at a threshold level over long periods of time and that there would be short periodical increases and recessions to account for ovulation, for the periods of expulsion of embryos from the ovary, and the intervals between them.

The fact that the older embryos are evacuated from the follicles and are expelled from the ovary while younger embryos are not, indicates that it is not contraction of the ovarian walls which ruptures the follicles. Neither are the follicles ruptured by movements of embryos. A

simultaneous rupture of follicles enclosing embryos of the same age indicates that a true ovulation occurs when the embryos are expelled from the follicles.

VIVIPAROUS FISHES WITH GESTATION IN THE OVARIAN CAVITY

It has been pointed out that one type of viviparity involves an early expulsion of embryos from the ovarian follicles and a long period of gestation in which the embryos are contained within the ovarian cavity. Embryos of the two families of the order Cyprinodontes, Jenynsiidae (Scott, 1928; Siccardi, 1940) and Goodeidae, pass their period of gestation in this manner. This type of viviparity is characteristic also of embiotocid fish (Eigenmann, 1892; Turner, 1938) and some brotulid fish (Stuhlman, 1887; Lane, 1903). In this type of viviparity fertilization occurs within the ovarian follicle. There is an early ovulation as a result of which the embryos come to lie in the ovarian cavity. A long period of gestation follows which necessitates a quiescent state in the muscle of the ovarian wall to prevent early evacuation of the embryos. At the conclusion of the period of gestation there is a reactivation of the ovarian musculature and birth takes place. The reproductive cycle in the Embiotocidae and in the viviparous brotulid fishes is an annual one. The goodeid fishes reproduce several times each year and there is a cyclical change in the tissues of the ovary itself accompanying this type of viviparity. In early gestation the epithelium of the ovarian cavity becomes glandular and the cells become columnar. Later this epithelium desquamates. There is some increase in the vascularity of the lining of the ovarian cavity in early gestation, but in middle and late gestation the vascularity increases greatly. The stroma of the ovary becomes spongy and swollen soon after the embryos have been expelled into the ovarian cavity. Later, with the general increase in vascularity in the ovary, the stroma shrinks. Most of these changes are temporary and cyclical in nature, but

the blood vessels, once their walls have become thickened, do not recede with the involution of the ovary.

Assuming again that a pituitary hormone has a follicular-stimulating effect in the female and that the processes of ovulation and muscular contraction also take place when the appropriate hormones reach a threshold level, a certain parallelism is seen between the control in annual oviparous fishes and in the annually reproducing embiotocid fish, *Cymatogaster*. Maturation of ova and expulsion of ova or early embryos occur in the same sequence and without much change in the time relations. However, in the oviparous fish, expulsion of ova from the body follows ovulation quickly, while the process is delayed for a period of five or six months in *Cymatogaster*, during which the embryos are developed in the ovarian cavity. Endocrine control of the ovarian musculature in the oviparous fish and in *Cymatogaster* must differ to the extent indicated by the length of time between ovulation and activation of the ovarian musculature for the expulsion of the embryos.

Since the reproductive cycle in *Cymatogaster* is an annual one and that of the goodeid fishes is repeated several times during each year, it may be assumed that there is some difference in the periodicity of the hormone responsible for follicular stimulation and the maturity of the eggs.

It is quite possible that the cyclical changes in the somatic tissue of the ovary are under hormone control independent of that which causes ovulation and quiescence of the ovarian musculature. Mendoza (1937) has found in goodeid fishes some evidence for regular periodical changes in the ovarian tissue in virgin females and in fishes which are not reproducing. This would indicate that the cyclical changes in the ovarian tissue are not altogether dependent upon the presence of embryos in the ovarian cavity.

Summary

The types of viviparity in teleost fishes involve differ-

ences in: (1) locati on within the ovary during gestation; (2) length of period of gestation and maturity of embryos at birth; (3) degree of dependence of embryos upon the maternal parent; (4) degree of modification of the ovarian tissue; (5) periodicity in reproductive cycles; (6) sequence in fertilization, ovulation, hatching, retention of ova or embryos and finally expulsion of embryos.

Some of the processes—at least development of ova, ovulation, retention of embryos and expulsion of embryos (birth)—are presumably under hormone control, and diversity in type of viviparity is therefore accompanied by an equivalent diversity in the hormones functioning in the control of reproduction.

LITERATURE CITED

Eigenmann, Carl H.
1892. *Bull. U. S. Fish. Comm.*, 12: 401–479.
Houssay, B. A.
1930. *Rev. de la Soc. Argentina de Biol.*, Vol. 6.
Hubbs, Carl L.
1921. *Biol. Bull.*, 40: 181–209.
Lane, Henry H.
1903. *Biol. Bull.*, 6: 38–54.
Mendoza, Guillermo
1937. Unpublished doctor's thesis, Department of Zoology, Northwestern University.
Scott, Maria Isabel Hylton
1928. *Anal. Museo Hist. Nat. de Buenos Aires*, Vol. 34 (Ictologia, publ. no. 13).
Siccardi, Elvira M.
1940. *La Prensa Medica Argentina.* T. XXVII, Nos. 38, 39.
Smith, Hugh M.
1926. *Trans. Amer. Fish. Soc.*, 56: 213–226.
Stuhlman, Franz L.
1887. *Abh. Naturw. Ver. Hamburg*, Bd. 10.
Turner, C. L.
1937. *Biol. Bull.*, 82: 2, 145–164.
1938. *Jour. Morph.*, 62: 2, 351–373.
1940a. *Jour. Morph.*, 67: 1, 59–89.
1940b. *Jour. Morph.*, 67: 1, 91–105.
1940c. *Jour. Morph.*, 67: 2, 271–289.
1940d. *Jour. Morph.*, 67: 2, 291–297.
Villadolid, Deogracias V., and Porfirio R. Manocop
1934. *Philippine Jour. Sci.*, 55: 3, 193–220.
Williamson, H. C.
1911. *Sci. Invest. of Fish. Board of Scotland for 1910*, no. 1.

GENES, SPECIES, VARIABILITY AND PLANT-BREEDING

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INTRODUCTION

FROM a plant-breeding standpoint the kinds, the amounts and the causes of variability are of the utmost importance. Plant genetics is primarily an attempt to explain the relations in kinds and causes, of progenies and parents in terms of characters. Fundamentally all variability is the product of gene action in one form or another, modified by differences in environment. Characters, then, always result from the expressions of a gene or genes in a given environment. Some genes or gene combinations are very sensitive to characteristic or usual expression alteration by various common environments such as differences in soil, temperature, light or water. Other genes or gene combinations are rarely thus affected.

Whether one considers genes as ultramicroscopic particles of protoplasm, a certain type of chemical reaction, or a shorthand term for describing certain experimental phenomena, matters relatively little to the practical plant-breeder. These may be, from this standpoint, three faces of the same phenomena, three pictures from different view-points. What is important are unit differences, the reactions and relations of which in terms of characters are subject to fairly accurate prediction in certain types of experimental and practical procedures.

Species, on what some may still regard as an assumption, are combinations of genes, and the differences between them are fundamentally gene differences, either qualitatively or quantitatively, just as practically every one recognizes varietal differences are. There is no sharp distinction. Plant experimenters and many plant taxonomists agree that such systematic units are convenient

but relatively unstandardized concepts—that species in one genus may not represent the same order of classification as those of another. Even species within the same genus may not be of the same order of magnitude. What is true of the species concept is still more apparent as regards the higher units of classification, such as genera and families. Some species, genera and families, however, are recognized as more "natural" groups than others, meaning, of course, that they have many more genes in common and that they, perhaps genealogically, arose from a common ancestor. It is more and more apparent, as genetic experimentation accumulates, that the variety, in the broadest sense, is the geneticist's systematic and experimental unit. Certainly it is and should be the practical unit of the plant-breeder. It is becoming increasingly difficult from an experimental standpoint to distinguish between varieties and species, since many species in one sense or another are hybrids, and since there are no clear differential criteria. In horticultural and agricultural publications, many varieties are often designated as species though they may be forms of a hybrid.

Variability, phenotypically considered, is much more common in some species, genera and families than in others. Certain characters are more liable to hereditary substitution than are others. In the succeeding discussion, it is not to be inferred that characters designated by the same name but occurring in different species, genera or families are expressions of the same gene or gene combination. Some of them may be; others I know are not. In listing taxonomic units as stable or unstable, the number of known named varieties within the so-called species, however caused, as well as the unnamed but known variations are considered.

In the case of the stable species listed, the data have come from observation of hundreds or, in most cases, thousands of plants either raised from seed at the Blandy

Experimental Farm during the last ten years or from general observations of plants in general cultivation or in the wild or from the absence of varietal designations in trade or scientific publications. *Convallaria majalis,* for example, has only four forms so far as I can discover, in cultivation or among wild plants in the southern Alleghenies, that are strikingly distinct. These are a pink-flowered type, a double-flowered type, the common type and a giant form. Yet this plant has been propagated by the millions through asexual division and occasional seed. In the wild, the numerous patches would indicate reproduction by seed.

Lathyrus latifolius, the perennial summer-flowering pea, though grown from seed by the millions, appears to have only four forms, and these are flower color types. This is in great contrast to its near relative, the common sweet pea, *Lathyrus odoratus.*

TABLE I

STABLE AND UNSTABLE SPECIES

Stable	Unstable
Convallaria majalis	*Zea mays*
Asparagus officinalis	*Phoenix dactylifera*
Lathyrus latifolius	*Ricinus communis*
Vinca minor	*Pisum sativum* incl.
Vinca rosea	*arvense* forms
Alyssum maritimum	*Phlox drummondi*
Ginkgo biloba	*Phaseolus vulgaris*
Sophora japonica	*Lathyrus odoratus*
Parkinsonia aculeata	*Thuja occidentalis*
Portulaca parana	*Picea abies (excelsa)*
Silene virginica	*Acer palmatum*
Silene orientalis	*Phlox subulata*
Pastinacea sativa	*Silene pennsylvanica*
Begonia evansiana	*Lagerstroemia indica*
Howea belmoriana	*Citrullus vulgaris*
Martynia lutea	*Cucumis melo*
Papaver dubium	*Rhaphanus sativum*
Nelumbium luteum	*Brassica oleracea*
Cassia marylandica	*Hibiscus syriacus*
Lilium regale	*Hedera helix*
Lilium tenuifolium	*Cucurbita pepo*
Alyssum montanum	*Lactuca sativa*

I have looked at more than a thousand flowering plants of *Silene virginica* scattered over a geographical area of several hundred miles, and among these I discovered only one easily noted variation, a duller red flower color.

Hundreds of plants of *Portulaca parana* have failed to show any easily observed variations, although the closely allied commonly grown species, *P. grandiflora,* is known by dozens of forms.

Thousands of plants of *Silene compacta* (*orientalis*) grown at the Blandy Experimental Farm have brought forth only one at all striking variation—a lighter flower color shade.

From several hundred to several thousand individuals of most of the other stable species listed have been under close observation with results indicating but a slight tendency to vary. *Asparagus officinalis* has been grown by the millions commercially from seed, yet the few varieties in cultivation, grown side by side, have differences only recognizable by experts, rust resistance being the most striking. One might add many more species to this list, judging by my observations on the Blandy Experimental Farm cultures and elsewhere.

As to the unstable species listed, these, with few exceptions, are represented in horticulture by a hundred or more varieties, involving many variations as distinguished from just different gene combinations. Species such as *Pisum sativum, Citrullus vulgaris, Cucurbita pepo, Brassica oleracea, Phaseolus vulgaris* and *Ricinus communis* are made up of hundreds of varieties, differentiated by characters so striking as to cause serious doubt as to whether it is good science to place them under one name. During the World War, I visited thousands of acres of *Ricinus communis* under cultivation. I also saw many spontaneous "wild" types in various parts of the United States. Dr. J. B. S. Norton, of the University of Maryland, sent me a collection of several hundred types he had collected for taxonomic study. Previously I had been engaged in studies on the genetics of this species

and had made a considerable collection of types. There were enormous differences in seed size, in plant height, in time necessary for maturing fruit, in length of life. Some types had a life span of less than four months, and died after maturing one crop of seed, just as any annual would. Other types lived at least three years, developed a trunk a foot in diameter and matured fruit seasonally, as do apples. Some so-called wild trees I saw on the Rio Grande were said to be 20 years old, and from observations on experimental cultures, I know they will live at least 3 years. Differences in sex expression ranged from normal monoeciousness to almost complete absence of pistillate flowers. In one plantation I saw over 50 acres of such a type. I could describe 50 different pairs of contrasting characters in this species, yet in my experimental work there was no difficulty in crossing the most extreme types, and no sterility was apparent. Similar striking differences occur in many of the other unstable species mentioned, but crosses between the numerous forms, in all the cases tried, have been easily effected, and no sterility appeared. Whitaker's work (1932, 1933) on crossing the bitter colocynth with the watermelon, and the orange and nest-egg gourds with forms of the common pumpkin are cases in point.

In a number of the species listed, such as *Lagerstroemia indica, Hibiscus syriacus, Silene pennsylvanica* and *Phlox subulata,* the variability is not indicated to any extent by named varieties.

Not only species but genera and, to a less extent, families, can be listed as relatively stable and unstable.

Stable genera are *Ginkgo, Sciadopitys, Vinca, Castanea, Callirhöe, Calystegia, Ipomaea, Ligustrum, Cercis, Albizzia, Platanus, Gelsemium* and *Howea* (*Kentia*).

Unstable genera are *Holcus* (*Andropogon*), *Oryza, Triticum, Pyrus, Rosa, Prunus, Papaver, Syringa, Lycopersicum, Gossypium, Epigaea, Iris, Lilium, Sedum, Juniperus, Phoenix* and *Thuja.*

By stability and instability in a genus is meant the

variability within the species of that genus rather than the number of species that comprise it, although this latter fact should also be considered. Most of the genera listed above as stable have relatively few species. In some of the unstable genera listed, one may conclude that natural or artificial hybridization between species is mostly responsible for their instability or great variability, but an examination of the character differences resulting from their instability shows that many of these are mutations and not new or different gene combinations in the ordinary sense.

Families that are relatively stable because their species in general produce few variations, except in exceptional cases, are *Punicaceae, Lemnaceae, Musaceae, Leitneriaceae, Resedaceae, Umbelliferae, Convolvulaceae* and *Martyniaceae.* Of these, the most unstable are the *Umbelliferae* and the *Convolvulaceae,* but this variability in these families is only marked in a very few species, such as the Japanese morning-glory and the common carrot, and both families are large in species number.

Unstable families are *Compositae, Cucurbitaceae, Rosaceae, Solanaceae, Scrophulariaceae, Gramineae* and *Nymphaeaceae.* Part of this instability undoubtedly has resulted from natural or artificial species and varietal hybridization, but the innumerable and striking character differences between the components of each of these families indicate much mutative phenomena. Any student of variation acquainted with the forms to be found among the species of these two groups of families can not help but be struck by the great contrast in their stability and instability.

Considering variability phenotypically among the various systematic groups, an examination makes it evident that some characters are rare and others are common.

Common variations among flowering plants are white flower from colored flower forms, fasciation from normal, colorless seed coat from colored, fastigiate and weeping habit from non-fastigiate and non-weeping types,

various chlorophyll defects, especially albino or yellow-leaved from green-leaved types, double flowers from single, cut or laciniate-leaved forms from non-laciniate types, purple-leaf from green-leaf forms, dwarf from tall, earliness from late flowering or fruiting types, annual from perennial and changes from a light skin color in fruit to a darker, more intense shade.

Rare variations are changes in flower color from non-anthocyanin to anthocyanin, tendrilled to non-tendrilled, normal to pistillody of stamens, catacorolla or outside flower doubling from non-catacorolla, indeterminate growth from determinate, simple-leaf and pitcher-leaved forms from compound and non-pitcher types, non-glaucous from glaucous, wrinkled seed from smooth seed types, non-parchmented pods from parchmented, and evergreen or persistent foliage from deciduous or *vice-versa.*

Certain types of character change or variation seem to be definitely associated with taxonomic units, as though their protoplasmic composition was such as to give rise to only certain expressions and not to others. In other words, genes or gene groups appear to be limited in their distribution so that some species, genera or families not only do not possess among their individuals certain characters, but perhaps do not have the fundamental possibility of having them under any condition.

The genus *Rosa* appears very limited in ability to produce blue-flowered forms, while the *Iris* genus is equally limited in regard to the production of crimson or scarlet-flowered types. The very large genus *Rhododendron* apparently insists on "acid" soils, never throwing variations that are lime-tolerant, although some species in this genus require a less "acid" soil than others. Related genera have produced species that are lime-tolerant—*Erica carnea, Arbutus unedo* and *A. texana.*

All these various groups of facts indicate that variability in different forms is in some manner limited both in direction and amount, and that some taxonomic units

are stable or unstable in much the same degree as are gold and radium. For the plant-breeder, this means that with the various tools and methods with which modern science has equipped him, he would be more successful in certain directions than others in reference to a given group. For the cytogeneticist, shooting a stable species into great variability should perhaps open up a new vista, since most of the investigations involving the "artificial" production of mutations have had to do with "naturally" unstable species.

Environment, to the modern plant-breeder, is extremely important, since he makes his combinations to fit certain niches—certain localities. Soil and nutrient materials have a well-known effect on such characters as color and size, fasciation, chlorophyll defects, dull flower colors, height. This is admirably illustrated by the effect of the soil constituents on the blue or pink flower color of *Hydrangea macrophylla* var. *hortensis*.

Temperature affects fruit and flower color intensities and flavors, especially as regards sugar content. It is also important in its effects on growth.

Light also effects color and growth characters, vitamin contents, time and length of flowering and fruiting periods and spans.

Water is important in altering size and flavor characters.

Disease resistance is very much bound up with environmental factors. There is some evidence that a definite blooming period may be changed to a continuous one by environmental conditions. *Magnolia grandiflora* is said to be practically ever-blooming in New Zealand, 10 or 11 months out of 12 (Thomson, 1931).

It is quite obvious that environmental phenomena are important considerations in any plant-breeding program and should be more prominently emphasized than is generally done in practical genetics literature. Many workers in horticulture and agriculture outside of scientific circles are quite ignorant of the relations between environ-

ment and heredity in the formation of plant characters. Only certain, not all varieties of hydrangeas, produce either blue or pink flowers, depending on the soil conditions. Environment in many cases can reduce certain tall forms to dwarfs or *vice versa,* which tried on other forms would be ineffective.

Variability, broadly considered, depends on three general phenomena: (1) the degree of gene stability or instability; (2) the gene pattern or the gene-make-up of the particular organism concerned; and (3) the effect of the external environment on particular gene or gene group expressions. Taxonomic units, such as varieties, species and genera, differ from each other through changes in chromosome gene patterns and the presence and absence of certain genes.

Emerson, Stadler, Demerec, the Drosophila workers and many others have demonstrated in many forms that genes differ in their stability or instability. Stadler has shown this to be strikingly true in *Zea mays* (1930, 1931), and Demerec (1931, 1933) in *Delphinium ajacis.* In Stadler's data, the frequency of change in seven genes of maize ranged 0 per million gametes for *Wx* to 492 per million gametes for *R.* In *Drosophila melanogaster,* according to Demerec (1933), "unstable genes" occur with a rather high frequency. In *Drosophila virilis* and *Delphinium* unstable genes occur at different rates in different stages of the organism's development. In some organisms, some genes are stable in somatic cells, unstable in germ cells. Gene changes are reversible, but occur more frequently from wild type or dominant to mutant than from mutant or recessive to wild type or dominant. So-called recessive mutations are many times more frequent than "dominant" mutations. Dominant and wild type are not synonymous, but practically so, since most wild-type characters are dominants. "Eversporting" characters of plants, particularly striping color patterns, are relatively common examples of unstable genes or gene groups. The presence of a long multiple

allelic series may be indicative of gene instability. Apparently some genes mutate into a *very* limited number of changes, while others have a much more extended repertoire, as judged by the allelic series of their loci. According to Demerec (1933), gene change "is not always a random process; it may be favored by certain tissues, or it may be limited to certain tissues." Demerec finds factors in *Drosophila virilis,* four of which increase rate of gene change in somatic cells and one that increases it in germ cells. There is little doubt but what this phenomenon is general. The impression exists from studies on *Drosophila* and maize that the majority of gene changes or mutations are some form of lethal. In x-ray produced changes in different loci of *Drosophila melanogaster,* Patterson (1929) found 86 per cent. lethals, the range for different loci varying from 15 lethals: 2 visibles to 20 lethals to 4 visibles.

Changes in the more unstable genes indicate the mutant to be more unstable than the wild type from which it originated (Demerec, 1933). This simply emphasizes the instability of some mutant genes as contrasted with other mutant genes.

By changes in gene pattern or gene make-up in a systematic unit, I do not mean changes in the gene itself or so-called point mutations, but modifications due to chromosome structural changes, such as segmental interchange, crossing over, deletion, translocation, inversion, fragmentation, duplication and various forms of ploidy, whether it be repetition of one chromosome type or of the whole set, and lastly new combinations of chromosomes brought about through hybridization. Recent studies (Goldschmidt, 1937; Stadler, 1932; Demerec, 1938) indicate there may be some foundation for regarding all changes in genes as structural changes in chromosome segments rather than chemical changes within a gene particle.

Since all genes express themselves in a given environment, environment as previously indicated may be a very

important cause of variability, although the changes produced by it are generally much less striking than those produced through changes in genes or gene patterns.

Actually it often becomes difficult or next to impossible to distinguish between environmental variations and so-called hereditary variations, without detailed experimentation. Not infrequently a plant blooms off season on a branch or shoot, disporting a few flowers. A decade or so ago, it would have been passed by without question as a result of abnormal weather or soil conditions. Such a phenomenon gave rise to the New Dawn rose, an ever-blooming sport of the Van Fleet rose. Van Fleet not infrequently does this. So do certain strains of Wisteria, *Phlox subulata, Forsythia viridissima* and certain varieties of pomaceous and drupaceous fruit trees. Some of these may be bud mutations, while others, perhaps the majority, may be simply called forth by particular environmental stimuli. Only experimental inquiry will determine which. Genetic investigation has taught us to be conscious of this state of affairs. It has taught us to attempt to study differences by trying to grow our plants in controlled similar environmental conditions, but in practice this is very difficult, because of our great ignorance. In other words, it is hard to know "beans when the bag is open." Many plantsmen, no doubt, saw the emergence of a New Dawn rose without being conscious of it. Only one took the necessary step that gave us the variety, and then it was so simple that one wonders how it was overlooked. Judging by recent studies of Shamel and Pomeroy (1932, 1936), bud mutation is a relatively common phenomena in many cultivated plants, showing many types of characters, of the same general order as those secured through seed or germinal mutations. Species and higher systematic units appear to show the same characteristic stability or instability as regards production of bud mutations as they do in regard to germinal mutations. *Portulaca grandiflora* bud sports, *Portulaca parana* remains stable. The cultivated Rosaceae, Compositae and

Citrus are notorious bud mutators, while *Asparagus, Convallaria* and *Vinca* stick to the ancestral traditions, though millions of plants have been grown asexually.

Ability to survive low temperatures has been demonstrated to be an inherited character and in some cases investigations have placed it on a gene basis. We have developed so-called frost-proof varieties of corn, pansies and other cultivated plants. What part environment plays in the manifestation of this character is as yet but vaguely sensed. Species growing naturally in relatively high temperature regions not infrequently survive in very much colder regions. In some cases this ability to survive is apparently true of many random samples of the species; in other cases it appears to be true of strains developed from certain individuals; as evidenced in our experiments with *Hibiscus coccineus* from the swamps of Georgia. We have a strain winter hardy at the Blandy Experimental Farm, and one that is not. We have had similar experiences with a number of other species, often differences occurring in seed from the same package, *e.g., Cupressus arizonica* or plants from a small purchased lot—Gerbera, *Chaemacyparis lawsoniana, Cunninghamia lanceolata.*

Ability of a species to survive lower temperatures is not necessarily indicated by what is true of another species native to that locality. The one species may have reached the limit of its endurance, while other species have been restricted to such temperature zones by an entirely different and unrelated set of environmental factors.

The Louisiana irises, involving *Iris fulva, Iris hexagona* and numerous natural hybrids, survive temperatures of −6 degrees F. or even lower at the Blandy Experimental Farm and are said to survive much lower temperatures at the New York Botanical Garden and Brooklyn Botanic Garden, if wintered relatively dry, though they are naturally swamp plants. Tubers of the chufa, *Cyperus esculentus,* if stored dry will survive

temperatures below zero, but if left in the ground, they invariably freeze.

An application of lime at Rothamsted made a striking difference in the winter survival of certain strains of alfalfa. Various observations indicate that a real possibility exists of materially and practically increasing the ability of plants to endure temperatures by modifying the environmental conditions.

The plant breeder of the past had relatively few procedures with which to work, and until Burbank and Mendel became part of the popular scene, small attention was paid to him. Many of his results were chance finds. Others resulted from a rather loose use of chance and conscious hybridization, selection, inbreeding and isolation procedures, but often with outstanding success.

The plant breeder of the present and future has a place alongside the engineer, the doctor and the lawyer. The available knowledge, procedures and "tools" have increased his opportunities enormously. Vast collections of plants are at his disposal with an amazing assortment of characters, together with great accumulations of very detailed information concerning their life histories and their intimate natures. He knows that species in the wild as well as under cultivation are collections of variables—strains and hybrids between them. He knows that two plants with the same name and apparently identical in character may when crossed produce new types. Not content with the variations at hand, he knows that in addition to the variability brought about by hybridization, it can further be increased artificially by x-rays, radium, centrifuging, aging of pollen and seeds, the use of colchicine, temperature and decapitation of growing shoots. Many of the variations thus produced may be seemingly useless, but he has an open mind. So many apparently useless discoveries have turned out remarkably otherwise. He has a much better appreciation of the importance of mass cultures, of wild cultures, more consciousness of both seed and bud mutations, and of what he is looking

for. He has ceased to be an orthodox hybridizer, and attempts to hybridize beyond what is often considered practical taxonomic limits by using high chromosome number forms for pistillate parents; by chromosome number inspections; by using bees to effect thousands of crosses to his one; by bringing together numerous forms, species, genera, etc., in great systematic collections, presenting an opportunity for natural hybridization with mass open-pollinated seed plantings and subsequent inspection; use of possibilities of close relatives and hidden factor combinations; trials of numerous techniques such as pollinating artificially shortened styles, enabling slow growing or short pollen tubes to reach the embryo sac before the flower parts wither or absciss; use of pollen mixtures—foreign pollen from species desired as parent with small per cent. of plant's own pollen, if self-fertile and many seeded ovary, to increase the possibility of the ovary developing to nourish the hybrid embryos; use of pollen mixtures from numbers of individuals of seed-propagated plants of same species or variety to overcome possible cross-incompatibility or other complications.

Having successfully effected hybridization, the modern plant breeder knows that there are lethal liabilities or hazards all the way from fertilized egg to mature fruiting plant, and that some of these may be overcome by artificial incubation of weak hybrid embryos (Laibach, 1929; Tukey, 1933), use of growth-promoting substances for propagating asexually weak hybrids, induction of polyploidy for overcoming certain types of sterility by the use of colchicine and hetero-auxin (Blakeslee, 1937, 1938; Nebel, 1938; Dermen, 1938; Greenleaf, 1938).

Finally he understands and appreciates some of the parts that parthenogenesis, apogamy and parthenocarpy might play in a plant-breeding program, *e.g.*, seedless watermelons and holly berries produced by spraying with growth-promoting substances (Wong, 1938; Gardner and Marth, 1937).

LITERATURE*

Anonymous
1938. From *Nature*, February 19, 1938, p. 340. *Jour. Heredity*, 29: 160.
Beadle, G. W.
1939. *Jour. Heredity*, 30: 245–247.
Blakeslee, A. F., and Amos G. Avery
1937. *Jour. Heredity*, 28: 393–411.
1938. *Collecting Net*, August 27, 1938.
Blakeslee, A. F., A. G. Avery, A. D. Bergner, S. Satina, H. E. Warmke, J. T. Buchholz, J. L. Cartledge and E. W. Sinnott
1938. Ann. Rpt. Dept. of Genetics, Carnegie Inst. of Washington, 1937–38, pp. 35–40.
Blakeslee, A. F.
1939. *Am. Jour. Bot.*, 26: 163–172.
Brierley, Philip, S. L. Emsweller and J. C. Miller
1937. *Proc. Am. Soc. Hort. Sci.*, 34: 603–606.
Bruman, A. J.
1937. *Jour. Heredity*, 28: 31–34.
Cates, J. Sydney
1938. *Country Gentleman*, 108: 23, 63, July.
Clausén, Jens, David D. Keck and W. M. Hiesey
1938. Carnegie Inst. of Washington Yearbook, 37: 218–222.
1939. *Am. Jour. Bot.*, 26: 103–106.
Cook, Robert C.
1937. *Jour. Heredity*, 28: 411–412.
Crane, M. B., and W. J. C. Lawrence
1938. "The Genetics of Garden Plants." 2nd ed., pp. xxi + 287. Macmillan, London.
Darlington, C. D.
1931. *Gardener's Chronicle*, 90: 351–353; 397–400; 447–448; 461–463.
Demerec, M.
1933. *Jour. Heredity*, 24: 369–378.
1938. Carnegie Inst. of Washington. Pub. 501, pp. 295–314.
Dermen, Haig, and George M. Darrow
1938. *Proc. Am. Soc. Hort. Sci.*, 36: 300–301.
Dermen, Haig, and D. H. Scott
1938. *Proc. Am. Soc. Hort. Sci.*, 36: 299.
Dermen, Haig
1938. *Jour. Heredity*, 29: 211–229.
Dobzhansky, Th.
1937. "Genetics and the Origin of Species." 364 pp. Columbia University Press. New York.
Dorsey, E.
1936. *Jour. Heredity*, 27: 154–160.

* The reference list was selected for its possible interest to plant breeders and is not to be considered in any sense complete.

Drain, Brooks D.
1932. *Mich. Agr. Exp. Sta. Tech. Bull.* 130, pp. 1–48.
Fitzgerald, O. A.
1938. *Country Gentleman,* 108: 23, 35, June.
Friend, W. H.
1934. *Jour. Heredity,* 25: 358.
Gardner, F. E., and P. C. Marth
1937. *Bot. Gaz.,* 99: 184–195.
Goldschmidt, R.
1937. *Nature,* 140: 767.
Goodspeed, T. H., and Fred M. Uber
1939. *Bot. Rev.,* 5: 1–48.
Greenleaf, W. H.
1938. *Jour. Heredity,* 29: 451–464.
Gustafson, F. G.
1936. *Rep. Proc. Nat. Acad. Sci.,* 22: 628–636.
Hall, A. D.
1931. *Gardner's Chronicle,* 90: 30.
Kostoff, D.
1935. *Compt. Rend. Acad. U.S.S.R.,* 2: 71–76.
1938. *Nature,* 142: 753.
Laibach, F.
1929. *Jour. Heredity,* 20: 200–208.
Lawrence, W. J. C.
1937. "Practical Plant Breeding." Pp. 155. George Allen and Unwin, Ltd. London.
Leighty, C. E., and W. J. Sando
1928. *Jour. Heredity,* 19: 23–27.
Levan, Albert
1939a. *Hereditas,* 25: 109–131.
1939b. *Hereditas,* 25: 87–96.
Lindstrom, E. W.
1932. *Jour. Heredity,* 23: 115–122.
1933. *Jour. Heredity,* 24: 129–137.
1936. *Bot. Rev.,* 2: 197–215.
MacArthur, John W.
1934. *Jour. Heredity,* 25: 75–78.
Mangelsdorf, P. C., and R. G. Reeves
1931. *Jour. Heredity,* 22: 328–343.
Michels, C. A.
1939. *The News Letter, Univ. of Idaho,* 22: No. 4, p. 2.
Nebel, B. R., and M. L. Ruttle
1938. *Jour. Heredity,* 29: 1–9.
1938. *N. Y. Agr. Exper. Sta.* (Geneva) Circ. 183.
O'Brien, Harry R.
1938. *Country Gentleman,* 108: 9, 56, January.
Patterson, J. T.
1929. *Jour. Exp. Zool.,* 53: 327–372.

Robinson, T. Ralph
1933. *Jour. Heredity*, 24: 437–439.
Romberg, L. D., and C. L. Smith
1938. *Proc. Am. Soc. Hort. Sci.*, 36: 161–170.
Ruys, B.
1931. *Gardener's Chronicle*, 90: 172.
Sando, W. J.
1935. *Jour. Heredity*, 26: 229–232.
Sansome, F. W., and J. Philp
1939. "Recent Advances in Plant Genetics." 2nd ed., pp. xii + 412. P. Blakiston's Son and Co. Philadelphia.
Shamel, A. D., and C. S. Pomeroy
1936. *Jour. Heredity*, 27: 486–494.
Smith, Harold H.
1939. *Jour. Heredity*, 30: 291–306.
Stadler, L. J.
1930a. *Jour. Heredity*, 21: 3–19.
1930b. *Anat. Rec.*, 47: 381.
1931. *Sci. Agr.*, 11: 645–661.
1932. *Proc. 6th International Congress Genetics*, 1: 274–294.
Stout, A. B., and E. J. Schreimer
1933. *Jour. Heredity*, 24: 217–229.
Stout, A. B.
1938. *Bot. Rev.*, 4: 275–369.
Thompson, Ross C., and W. F. Kozar
1938. *Proc. Am. Soc. Hort. Sci.*, 36: 641–644.
Thomson, W. M.
1931. *Gardner's Chronicle*, 90: 216.
Tukey, H. B.
1933. *Jour. Heredity*, 24: 7–12.
Verner, Leif.
1938. *Proc. Am. Soc. Hort. Sci.*, 36: 415–422.
Verushkine, S., and A. Shechurdine
1933. *Jour. Heredity*, 24: 329–335.
Wetmore, R. H., and Albert L. Delisle
1939. *Am. Jour. Bot.*, 26: 1–12.
Whitaker, T. W.
1932. *Jour. Heredity*, 23: 427–430.
1933. *Bot. Gaz.*, 44: 780–790.
White, Orland E.
1918. *Jour. Heredity*, 9: 195–200.
1925. *Mem. Brooklyn Bot. Garden*, 1: 513–521.
Winge, O.
1938. *Proc. Linnean Soc.*, 1937–1938. Pt. 4, 30 Dec., pp. 231–238.
Wong, Cheong-yin
1938. *Proc. Am. Soc. Hort. Sci.*, 36: 632–636.
Yearbooks
1936, 1937. U. S. Dept. Agr. Washington, D. C.

REVIEWS AND COMMENTS

EDITED BY CARL L. HUBBS

IN this section reviews and notices are given of current publications on general biology and of specialized works which have an important bearing in this general field. Emphasis is given to books and major articles which fall within the special scope of THE AMERICAN NATURALIST, in that they deal with the factors of organic evolution.

REVIEWS AND COMMENTS are meant to include also such general discussions, reports, news items and announcements as may be of wide interest to students of evolution. Except as otherwise indicated, all items are prepared by the Section Editor, Dr. Carl L. Hubbs, University of Michigan, Ann Arbor, Michigan. All opinions are those of the reviewer.

The Genetic and Endocrine Basis for Differences in Form and Behavior. As Elucidated by Studies of Contrasted Pureline Dog Breeds and Their Hybrids. By CHARLES R. STOCKARD and collaborators, with special contributions on behavior by O. D. ANDERSON and W. F. JAMES. Philadelphia: Wistar Institute of Anatomy and Biology, 1941: i–xx, 1–775, frontisp., pls. A, 1–112, figs. 1–128. $7.50.

THIS book presents the long-awaited results of an investigation which has been outstanding in support, scope and significance. It is a monument and a tribute to the leader and main author, who died in 1939. Dr. Stockard had largely completed the manuscript, but certain deficiencies remain. It is merely hinted that normal and pathological differences in size, form and behavior in man are correlated with the endocrines as well as with the genes, that similar constitutional types are exhibited by the breeds of dogs, and that the experimental study of these correlations in dogs may well be expected to throw light on the nature and diseases of man. The several phases of the research have not been masterfully integrated or summarized. There are some weaknesses in the genetic and the statistical treatments. Though regretting these deficiencies, scientists in many fields will find in this large book a wealth of data and interpretation. It will undoubtedly rank as one of the major biological contributions of the decade.

Although this study on the relation of the genes and the endocrines to the form and the behavior of dogs was un-

dertaken in the hope of elucidating problems in human biology and therapeutics, it also raises questions of fundamental significance in evolution. A central query runs throughout the book: Is the correlation that generally holds between the morphological and behavioral types of dogs due to a common ontogenetic cause, presumably lying in the endocrines, or does that correlation result from selective breeding, whereby independent changes in form and in physiology have been associated? Diverse combinations of form and behavior in dogs undoubtedly fit them, or once fitted them, very well to man's varied needs and whims. Strikingly parallel correlations between structures and functions characterize the many adaptations which allow animal kinds to persist in the struggle for existence. Bulky and armored creatures, for example, are closely bound to a solid substratum, commonly rely on protective resemblance to the environment, and are sluggish in their behavior; stream-lined animals are free-roving, and possessed of a highly responsive physiology. Each type is highly evolved; its characters are adaptive; the diverse adaptations are compensative. A correlation of the structures of either type with the functions of the other type would be disharmonious, antiadaptive. The bulky, protectively colored creature would not get along well if forced by inner urges to move about much or fast; an evolutionary line which has given up almost all other special protective devices to perfect a stream-lined form could not survive long if deprived of the neurophysiological basis for rapid responses. It becomes increasingly apparent, as a corollary of the modern Darwinian concepts of evolution, that structures and functions are harmoniously correlated.

A very basic problem, one on which Stockard's work has a profound bearing, is whether evolution in these form–behavior correlations involves independent genetic changes, or single mutations which effect both structure and function in a definite way. Must progress toward

perfection in any given form–behavior correlation await a succession of independent mutations and selections? In that event the changes would need be small and alternating, to avoid overthrowing the harmonious balance between structures and functions, and between the organism and its environment. Such a process would surely be long, devious and inefficient. Can this evolutionary inefficiency be avoided by some mechanism which, through single genetic changes or a series of homologous changes, will effect progressive, harmonious adjustments (specialization)? Do the endocrines provide such a means, for phylogenetic as well as ontogenetic regulation of form and behavior? Do mutations affecting the hormones permit short-cuts to be taken toward evolutionary changes which involve a balance between structures and functions? If so, is not the relatively rapid evolution of the vertebrates a result (and perhaps a cause) of their special endocrine endowment?

No clear evidence that such an evolutionary mechanism exists is presented in the masterpiece under review. The data of Stockard and his associates strongly indicate, on the contrary, that the bodily, glandular and behavioral characters are largely independent in their genetic basis, although they are now harmoniously correlated in the various breeds of dogs as a result of selective breeding. Disharmonies result from hybridization, when the genetic factors segregate. Some of the most extreme and obvious of the maladjustments, such as malocclusion of the teeth, and the development of extremely short mandibles in long-muzzled dogs, are obviously disadvantageous and would ordinarily be selected against. Less extreme or less obvious disharmonies, such as most of the unusual correlations of bodily structures, glandular types and behavioral patterns, have apparently also been eliminated in the production of the pure breeds. Disharmonious constitutions seem to have been similarly set aside in natural selection. May we not conclude that the gradual

attainment of a harmonious balance, between genes and hormones, between structures and functions, in fact between all elements in the organismic whole, has been a major phase of evolution?

Speciation in the Avian Genus Junco. By ALDEN H. MILLER. Univ. Calif. Publ. Zool., 44, 1941: 173–434, figs. 1–33. $3.00.

UNLIKE most earlier studies undertaken at the Museum of Vertebrate Zoology this one is not limited to California and adjacent areas, but treats a systematic unit throughout all parts of its wide range, from the Arctic to Panama and from the Pacific to the Atlantic. This comprehensive coverage, the thoroughness of the investigation, and the breadth of the modern biological background, have combined to produce a noteworthy advance in the attack on the problems of speciation.

The original and objective treatment evident through this research on speciation in juncos is a welcome contrast to the rather crystallized, subjective approach that is common in ornithology. Statistical analysis is generally utilized, even for characters (such as the intensity of pigmentation in certain areas), for which successive stages, as determined by inspection, are assigned numbers on an arbitrary scale (colorimetric determinations—time-consuming and perhaps impracticable—would have rendered these analyses still more objective and precise). An experimental approach was attempted (unfortunately with limited results), as a supplement to years of broad, penetrating and coordinated observational research, in museums and afield. Sound, conservative judgment is employed in the interpretation of the varied data.

Students of general systematics who have regarded the speciational philosophy of many ornithologists as unduly simplified and rigid will welcome the clear indications that systematic relations in the genus *Junco* are decidedly complex. Widely different stages of isolation are involved and the several subspecies and species exhibit

various degrees of integrity and of distinctness. Several subspecies are demonstrated to be clusters of local races (called "divisions," "subdivisions," "subraces" and "colonies," since Miller follows general ornithological custom of synonymizing "race" with subspecies). "Colonial differentiation," some of it out of line with the general character gradients, is repeatedly recognized. Some subspecies are weakly separable (the percentage of specimens that are identifiable on set criteria is computed), whereas others are almost fully differentiated. It is admitted that the distinction between subspecies and species is at times arbitrary, and I suppose that ornithologists of the Kleinschmidt school will regard some of Miller's species as members of a single formenkreis.

Intermediate populations are classed as (1) subspecific ("interracial") intergrades or (2) interspecific hybrids—but no sharp criteria were discovered for the distinction of these categories. Two forms may intergrade in some localities but elsewhere may live together in pure form. Intergradation is recognized as of either the conventional geographic type or as "structural" (the intergradation in characters that is shown by incompletely differentiated forms which are prevented by isolation from interbreeding). Circumstances indicate that subspecific intergradation may either reflect an incomplete differentiation (I would call this antecedent or primary intergradation) or result from a new interbreeding between two forms which had previously been isolated and completely differentiated (subsequent or secondary intergradation). The transition between two forms may take place (1) gradually over a very wide area, so that the typical subspecies are recognizable only at the extremes of distribution; (2) in a transverse strip intervening between two broad ranges; (3) along a narrow mountain range connecting the two ranges; or (4) in small, isolated areas interpolated between the habitats of the parent forms.

In general the color varies in "seeming response to climatic gradient of increasing moisture and humidity: (1) replacement of eumelanin by phaeomelanin, and (2) intensification of such eumelanin as persists." Variations without such coordination, or involving reversed environmental correlation, are thought to have a historical explanation. "Gloger's Law of increased phaeomelanin and reduced eumelanin in dry hot climates finds unsatisfactory confirmation. . . . The evidence for [latitudinal] size differentiation in accordance with Bergmann's Law is unsatisfactory or wanting. . . . Relatively increased tail, foot, and bill lengths (Allen's Law) in southern members . . . can not be proved." Some characters are regarded as environmental adaptations; others are not. "Intermediate differentiation"—independent adaptation to intermediate climatic conditions—is hypothecated to explain some but not all of the form-gradients.

The races of juncos in general show a linear seriation, and many but not all of their characters are aligned into gradients (a term quite as satisfactory as Huxley's "clines"). Some gradients transcend species lines, as where two resident forms are separated by a barrier of low-altitude conditions. Intergradation in all varying characters often takes place in the same area, but in certain long, even gradients the several characters are most abruptly changed at different locations. The point of transition may even be different for males and females.

Character gradients are well graphed, and geographical relations are accurately mapped. Geographical consistency is stressed in all systematic and speciational considerations. Measurements and color features are well indicated in figures and tables, but there is not a single picture of a junco.

A bit of phyletic dreaming is indulged in, but the author is far too self-critical to follow the common custom of preparing a map, on which all forms in their present ranges

are connected by arrows to indicate origin and direction of evolution. Rather, alternative theories are advanced, to suggest possible modes of origin and differentiation.

A modern genetic view-point is maintained. An attempt is made to determine the genetic status of the characters of natural hybrid stocks. Some degree of segregation is indicated for certain characters, multiple-factor blending for others (size relations in particular). Genetic interpretations were largely based on circumstantial evidence, such as the ratios of color types observed in collections; but some of the evidence, as for the dominance of certain back and bill colors, was confirmed by the few successful experimental matings. From the ratios a forced effort was made to estimate the number of factors involved in certain color characters. Recurrent mutations are hypothecated, as one explanation for the striking variability exhibited by juncos. Two theories advanced to account for the rare occurrence in certain forms of characters more proper to other subspecies are (1) a gradual spread of mendelizing genes through the populations, and (2) interbreeding with migratory stragglers of other subspecies or species. Ability to hybridize is stated to be particularly dubious as a sole criterion of specific differentiation. Sporadic hybridization is thought to have been a factor in the modification of races (that is, in subspeciation), and certain forms which have developed a consistency in characters and in range are plausibly interpreted as having originated in subspecific intergradation or in interspecific hybridization. Contrary to the views of Goldschmidt, minor races and subspecies are treated without qualification as incipient steps in the origin of full species.

NOTICES OF NEW BOOKS

Genetics and the Origin of Species. Second Edition, revised. By THEODOSIUS DOBZHANSKY. New York: Columbia University Press, 1941: i–xviii, 1–446, figs. 1–24. $4.25.—The appearance of

a second edition of "Genetics and the Origin of Species" only four years after its first appearance testifies to the prominent place this treatise has taken in modern evolutionary thought. The revision continues on the progressive forefront, in that it further emphasizes the growing field of population genetics and treats other new developments in genetics and evolution.

Cytology, Genetics, and Evolution. By M. DEMEREC, CHARLES W. METZ, FRANZ SCHRADER, ALBERT F. BLAKESLEE, TH. DOBZHANSKY, CLARENCE E. MCCLUNG, HERBERT S. JENNINGS, WILLIAM F. DILLER, T. M. SONNEBORN, LEON CHURNEY, WILLIAM R. DURYEE and PAUL S. HENSHAW. Philadelphia: University of Pennsylvania Press, 1941: 1–168, 50 figs. $2.00.—The galaxy of authors will assure all that this summary treatment of cytological, genetical and evolutionary problems is authoritative, broad and up-to-date.

The Microbe's Challenge. By FREDERICK EBERSON. Lancaster, Pa.: Jaques Cattell Press, 1941: i–viii, 1–354, 3 pls., 1 fig. $3.50.—This is the story of the struggle that top-ranking human minds have waged against man's all but invisible enemies, and of the microbes' capacity to fight back. It is well and interestingly written, understandable to all and authoritative.

The Biochemistry of Symbiotic Nitrogen Fixation. By PERRY W. WILSON. Madison: University of Wisconsin Press, "1940" [1941]: i–xiv, 1–302, pls. 1–34, figs. 1–27.—This thorough treatment of nitrogen fixation by the Leguminosae is of decided concern to students of symbiosis as well as to biochemists and agriculturists.

SHORTER ARTICLES AND DISCUSSION

WINTER REDUCTION OF SMALL MAMMAL POPULATIONS AND ITS PROBABLE SIGNIFICANCE

THE causes for the fluctuations of certain animals has received much study in recent years. This is particularly true of small mammal populations. Several species which compose these populations show wide fluctuations in numbers from one year to the next.

In order to study the mechanics of cyclic populations and to properly evaluate the causes which allow for such drastic population reductions and rapid recoveries, it is desirable to collect sizable series at rather regular intervals throughout the year. Only in this manner can suitable samples be obtained for study and analyses of the various factors operating to bring about these cycles.

In eastern United States, various species of small mammals, such as the deer mice (*Peromyscus leucopus* and *P. maniculatus*), red-backed mice (*Clethrionomys gapperi*), long-tailed shrews (*Sorex fumeus* and *S. cinereus*), short-tailed shrew (*Blarina brevicauda*) and woodland jumping mouse (*Napaeozapus insignis*) are found abundantly in forested regions, occupying the substratum of the forest floor, where thick leaf mold and friable soil permit the construction of tunnels and burrows. Here small mammals are at times unbelievably abundant, while at other times they may be notably scarce.

As previously stated, it is desirable in population studies to secure representative samples of each species throughout the year. This is not always possible during the winter, when a deep snow cover may exist for several months, making trapping most difficult and resulting in the capture of relatively few specimens.

It has been our practice to run trap lines in extensive tracts of woods with similar flora and soil characteristics. During the first week of October, lines of 200 traps each are placed over a 1/4 mile stretch for a period of 5 days, the traps being bunched in groups of 5–10. Similar lines are run during the first week of May, under the same conditions. Walnut meat bait is used both in the fall and spring. Several such lines are run concurrently. We thus have comparable data on three or four thousand trap nights in the fall and again in the spring.

When the total catches for the fall and spring periods are compared, a notable difference is at once apparent. The catches in the fall of the year may be two to five times greater than those of the following spring (Fig. 1).

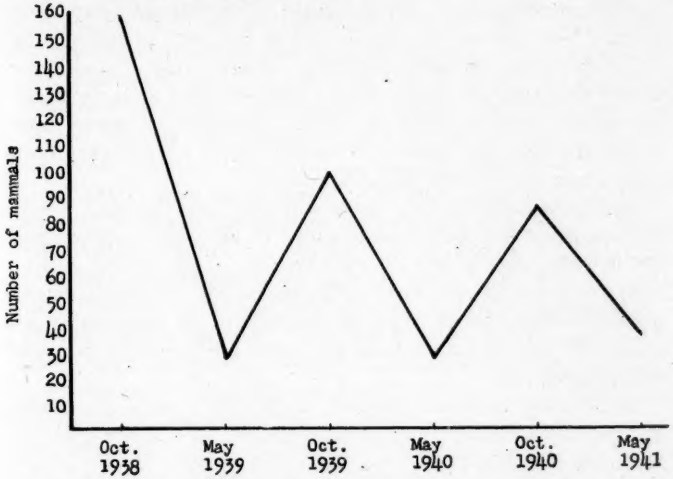

FIG. 1. Population reduction of small mammals on a thousand foot trap line (1000 trap nights) from October to May during three consecutive years.

The cause of this decline is not so apparent as might appear. Perhaps the most obvious reason for this decline would be the natural death rate during a period when the population is not being replaced by breeding individuals. This might occasion some decline, as it probably does, but surely it is insufficient to account for a reduction of nearly 80 per cent. of the population in some years.

Another probable cause for the drastic reduction might be found in lessened food, resulting in actual starvation or at least a minimum fare which is insufficient to maintain the species throughout the winter. We can not subscribe to this view when we consider that all specimens taken during the winter months have had well-filled stomachs and intestines and have appeared in first-rate physical condition. Moreover, examination of the leaf mold and the ground strata occupied by these species shows a varied assortment of foods naturally consumed by the small mammal population.

Severe weather, with attendant subzero temperatures, can hold

little dread for the small mammal population. In the forest, snowfall is a benefit, tending to insulate the soil and probably acts as a distinct asset in lessening predation.

We can point to only one probable cause that appears to favor this winter reduction. Briefly stated, it is that, in most small mammal populations, there is a distinct turnover of the population each winter, the adults of many species dying of senility or some other cause after they have passed through a single breeding season. The majority of shrews, deer mice, jumping mice, red-backed mice and species of similar size die when they have attained an age of from 15 to 22 months.

Those who object to this thesis will point out the instances in which captive deer mice have attained an age of 5 years or more (Dice, 1933) and a few isolated records of microtines having lived two years in captivity. The limitations on natural breeding and activity which captivity imposes might conceivably act against the species maintaining its usual high metabolic rate, and thus prolong life.

On the other hand, we have positive evidence that some shrews, such as *Sorex fumeus* (and perhaps others) have a life span seldom exceeding 14–17 months (Hamilton, 1940). There is substantial evidence that field mice (*Microtus*) likewise seldom live more than 18 months, or two years at the most, death from old age occurring during the winter months (Hamilton, 1937). Moreover, we now have evidence from live-trapping records which indicate that, wherever trapping has been conducted from one year to the next, very few, if any, marked specimens are taken in the year following that of their first capture, particularly if these individuals were adult breeding animals when first captured (Burt, 1940). Finally, April and May captures are notable for the lack of fully mature or old individuals, those which may be considered to have bred at the beginning of the breeding season during the preceding year.

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LITERATURE CITED

Burt, W. H.
1940. *Misc. Publ. Mus. Zool. Univ. Michigan*, No. 45: 1–58.
Dice, Lee R.
1933. *Jour. Mamm.*, 14: 147–148.
Hamilton, W. J., Jr.
1937. AM. NAT., 71: 500–507.
1940. *Zoologica*, 25: 473–492.

A STUDY OF THE INTERACTION OF ALLELES AT THE EYELESS LOCUS

THE eyeless locus on the fourth chromosome of *Drosophila melanogaster* offers exceptional opportunity for the study of interaction of alleles, since six recessive alleles have been reported at this locus, as well as two dominant alleles. The present study was planned to show the effect on the eye of the combination of some of these alleles. For this purpose the following alleles were chosen: eyeless (ey), eyeless^2 (ey^2), eyeless-Russian (ey^R), eyeless-Dominant (ey^D), and eyeless-Dominant 39k (ey^{D39k}).

All stocks were made isogenic with each other by replacing all except the fourth chromosome with chromosomes from an inbred Oregon-R wild-type stock by the use of dominant markers and crossover suppressors. The isogenic stocks were then crossed to each other in such a manner that all possible combinations of alleles could be studied. In order to mark the chromosomes in the crosses, an isogenic stock of cubitus-interruptus-Dominant (ci^D) was used. The eye size of each allele and each combination of alleles was determined by classifying the eyes separately into the following classes: no eye, very little, one eighth, one fourth, one half, three fourths, nearly full and full. The classes were arbitrarily assigned the following values: 0, 1, 2, 4, 8, 12, 14 and 16, respectively. The final eye size recorded is the mean eye size derived from at least 50 eyes classified. The standard error of the mean is recorded for those cases used in deriving the conclusions. All experimental cultures were raised at 28°.

The data run as follows, with the male preceding the female in each case:

ey/ey	ey^2/ci ey^R	ci ey^R/ci^D (semi-
12.4	12.9	16 lethal)
11.3 ± 0.48	12.8 ± 0.64	16
ey/ey^2	ey^2/ey^D	ey^D/ey^{D39k}
13.2	8.4	11.7 ± 0.82
13.9	9	11.7 ± 0.90
ey/ci ey^R	ey^2/ey^{D39k}	ey^D/+
12.1	14.2	9.1
10.8 ± 0.73	14.5	9.3 ± 0.60
ey/ey^D	ey^2/+	ey^{D39k}/ey^{D39k}
7.8 ± 0.57	16	10.9 ± 0.56
6.6	16	14.8 ± 0.22

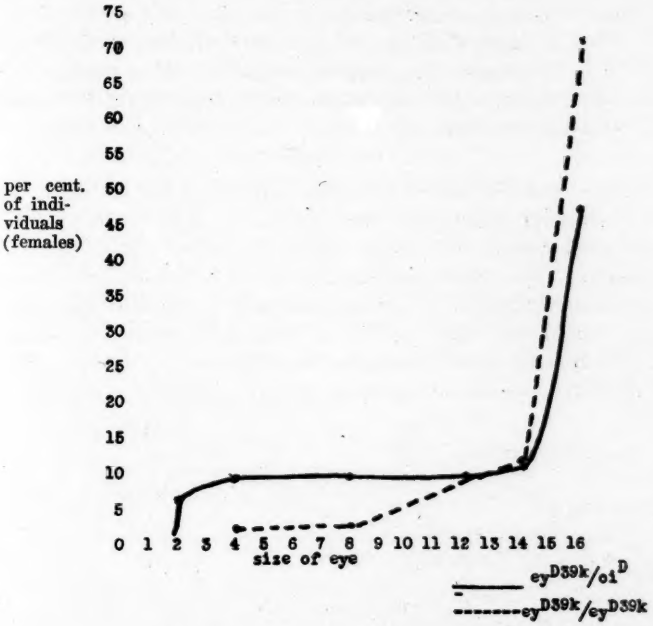
ey/ey^{D39k}	ey^2/ci^D	ey^{D39k}/ci^D
15	16	8.8 ± 0.47
15.4	16	12.2 ± 0.38
$ey/+$	ci ey^R/ci ey^R	$ey^{D39k}/+$
15.8	13.4	9.5
16	14.4 ± 0.23	12.6
ey/ci^D	ci ey^R/ey^D	$+/+$
16	7.7	16
16	9.1 ± 0.31	16
ey^2/ey^2	ci ey^R/ey^{D39k}	$+/ci^D$
13.2	13.7	16
14.3 ± 0.22	14	16
	ci $ey^R/+$	
	16	
	16	

The data indicate that the recessives interact with each other very much as though they were the same allele, there being no significant difference between the homozygotes of the three alleles or the heterozygotes between them. The ey allele is slightly dominant to wild-type; ey^R was partially dominant to wild-type before it was made isogenic (also observed by Bridges, 1935), but is recessive in the isogenic cross. There seems to be no difference in the phenotype of ey^D when heterozygous for ey^2, ey^R or the wild-type allele. ey^D/ey^{D39k} is smaller than $ey^{D39k}/+$ and is probably not significantly different from $ey^D/+$. Wherever ey^D appears the eye is a given size except in the case of ey/ey^D; it is possible that here ey^D is acted upon by ey to increase its limiting ability. The fact that ey/ey^D is smaller than $ey^D/+$ is in agreement with the data of Patterson and Muller (1930). Little indication of sexual dimorphism is shown by the recessives or by ey^D. Eyeless-D39k, however, acts differently from ey^D. In the homozygote or the heterozygote for wild-type the females have a larger eye than the males, but this dimorphism disappears when ey^{D39k} is heterozygous for a recessive allele.

Eyeless-D39k appears to be a hypomorph (terminology from Muller, 1932), performing the same role as the wild-type gene, but less efficiently, as indicated by a comparison of the heterozygote with the homozygote. This difference is shown to be significant when the distribution curves (Fig. 1) of the two are compared by making a two-row contingency table and applying a chi-square test (P = less than 0.01).

The distribution curves are especially significant since the two

differ mainly at the ends of the range where there is little difficulty or subjectivity in classification. A larger per cent. of the homozygotes have full eyes and none have eyes as small as do some of the heterozygotes. A full eye is unmistakable since it is per-



fectly formed, while an eye "nearly full" has a section unformed or an area of disarranged facets. Thus, two doses of ey^{D39k} give a larger eye than a single dose, and furthermore, a larger eye is obtained when any recessive is added to ey^{D39k}. It appears that in the case of these alleles, the more mutant material present, the more efficiently the eye is differentiated. Perhaps the reason why ey^{D} does not behave as a hypomorph is that it is inseparable from a duplication (Bridges, 1935a) and thereby differs from the other alleles. The fact that ey^{D} is not hypomorphic is supported by the observation of Rapoport (1938) that $ey^{D}/ey^{D}/+$ is the same as $ey^{D}/+$ and $ey^{D}/+/+$. Eyeless-D seems to limit the size of the eye rather than to inefficiently perform the role of the wild-type gene as does ey^{D39k}.

It is clear that these data represent conditions which have no

exact parallel in previous findings. As the problem stands, any explanation is bound to be entirely hypothetical. Some kind of double action does seem involved—one to cancel or modify the action of the wild-type gene (or complex of genes), and second to act positively in that the mutants perform a similar function to that of wild-type, only less efficiently.

I wish to express my appreciation to Professors L. C. Dunn and Th. Dobzhansky for helpful suggestions in planning the experiment, and to them as well as to Professor Franz Schrader for valuable criticisms.

SUMMARY

Three recessives and two dominant alleles at the eyeless locus in *Drosophila melanogaster* were crossed so as to obtain all possible combinations and the eye sizes of the various genotypes were classified. The results indicate that ey^{D39k} is hypomorphic since when homozygous or in combination with a recessive allele the eye is larger than that of $ey^{D39k}/+$. Eyeless-D, on the other hand, is not a hypomorph but limits the size of the eye. A double action is suggested as a possible explanation for the behavior of ey^{D39k}.

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LITERATURE CITED

Bridges, C. B.
1935. *Biol. Zh.*, 4: 401.
1935a. *Trud. Dinam. Razvit.*, 10: 463.
Muller, H. J.
1932. *Proc. 6th Int. Congr. Genet.*, 1: 213.
Patterson, J. T., and H. J. Muller
1930. *Genetics*, 15: 495.
Rapoport, J. A.
1938. *Biol. Zh.*, 7: 661.

AN ADAPTATION IN *AMBYSTOMA OPACUM* EMBRYOS TO DEVELOPMENT ON LAND

IN a series of determinations of density of embryonic tissues (Brown, Hamburger and Schmitt, 1941) it was found that the prospective neural tissue of *Ambystoma opacum* had a markedly lower density than the corresponding tissue of *A. maculatum, A. tigrinum* or *Rana palustris.* This lower density is indicative of a greater water-holding capacity of the tissue of *A. opacum* than in the tissue of the embryos of the species which lay their eggs

in the water. It appears to be a physical-chemical adaptation to development of the embryos on land.

Dissections in all cases were made in 0.6 Holtfreter solution, which is approximately isotonic with the capsular fluid of *A. maculatum* (see Richards, 1940). The osmotic pressure of the capsular fluid of *A. opacum* has not been determined, but, under the conditions under which development takes place, it is probably higher than the 0.6 Holtfreter solution so that in the natural place of development the water content of the prospective neural tissue may well be reduced to that of the related species which naturally develop in pond water.

The density of *A. opacum* prospective neural tissue was found to be close to 1.060 in comparison to close to 1.080 for *A. maculatum*, *A. tigrinum* and *R. palustris*. If this difference is through differences in osmotic pressure alone, then the osmotically active units in prospective neural tissue would be 33 per cent. greater per unit dry weight in *A. opacum* than in the other species.

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LITERATURE CITED

Brown, M. G., V. Hamburger and F. O. Schmitt
1941. *Jour. Exp. Zool.*, in press.

Richards, O. W.
1940. *Jour. Exp. Zool.*, 83: 401–406.

EFFECTS OF HUMIDITY ON DROSOPHILA MELANOGASTER PUPAE[1]

THE following experiments were undertaken for the purpose of comparing the effects of humidity on several mutants of *Drosophila melanogaster*. Pupae were exposed to various percentages of humidity and data obtained regarding the number of flies developing as well as the phenotypes of the survivors. Single pupae were placed in perforated No. 1 gelatine capsules. Groups of 25 capsules were placed in bags of cheese-cloth and suspended in half-pint milk bottles containing the desired humidities; 100 per cent. relative humidity was obtained by partially filling a bottle with water and closing it with a rubber stopper. Placing

[1] A contribution from the Department of Biology, the Catholic University of America, Washington, D. C. This paper, prepared under the direction of D. C. Braungart, instructor in biology, is based on the author's dissertation submitted in partial fulfillment of the requirements for the degree of master of science.

anhydrous calcium chloride in another stoppered bottle produced 0 per cent. humidity, and an intermediate humidity of 64 per cent. was obtained by using a saturated solution of sodium nitrate. For measuring the humidity an instrument in the form of a Reynault dew-point apparatus was found suitable.

The strains of Drosophila experimented with were wild, eyeless, vestigial and attached-X. A total of 175 pupae of each strain were subjected to each of the three humidities. Of the 2,100 pupae 1,160 developed into adults. The 100 per cent. humidity was optimal for the development of Drosophila, and lower humidities greatly increased the mortality. The observed per cent. survival of wild type compares closely with the results obtained by Elwyn.[2] Of the four strains, wild type showed the greatest survival in each of the humidities. The attached-X strain was next in hardiness. While vestigial was above eyeless at 100 per cent. and 64 per cent. humidities, it fell below eyeless at 0 per cent. A summary of the data is presented in Table 1:

TABLE 1

	Per cent. Survival		
	100 per cent. humidity	64 per cent. humidity	0 per cent. humidity
Wild type	89.0 ± 4.2	86.3 ± 1.9	53.7 ± 7.6
Attached-X	80.0 ± 2.7	71.0 ± 5.9	30.8 ± 4.8
Vestigial	79.0 ± 3.2	52.0 ± 3.5	0.6 ± 0.3
Eyeless	73.0 ± 5.2	38.3 ± 4.9	10.9 ± 1.9

Pupae less than two hours old were subjected to the three humidity conditions. Some of the pupae at 100 per cent. humidity acquired a green mold, and this evidently prevented their development. Nevertheless, the number of pupae developing at 100 per cent. humidity was greater than the number developing at lower humidities.

Many of the flies that hatched at 0 per cent. humidity were found to have folded wings. In addition, about 8 flies, including wild type and attached-X females, showed a change of color in the scape of their antennae. Instead of being the color of the fly's body, the scape was coal black. Neither folded wings nor the black scape proved inheritable. Since the experiments were performed in a room in which a 20° C. temperature was constantly maintained, the above-mentioned modifications were apparently due to lack of moisture.

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[2] *Bull. Amer. Mus. Nat. Hist.*, 37: 347–353, 1917.